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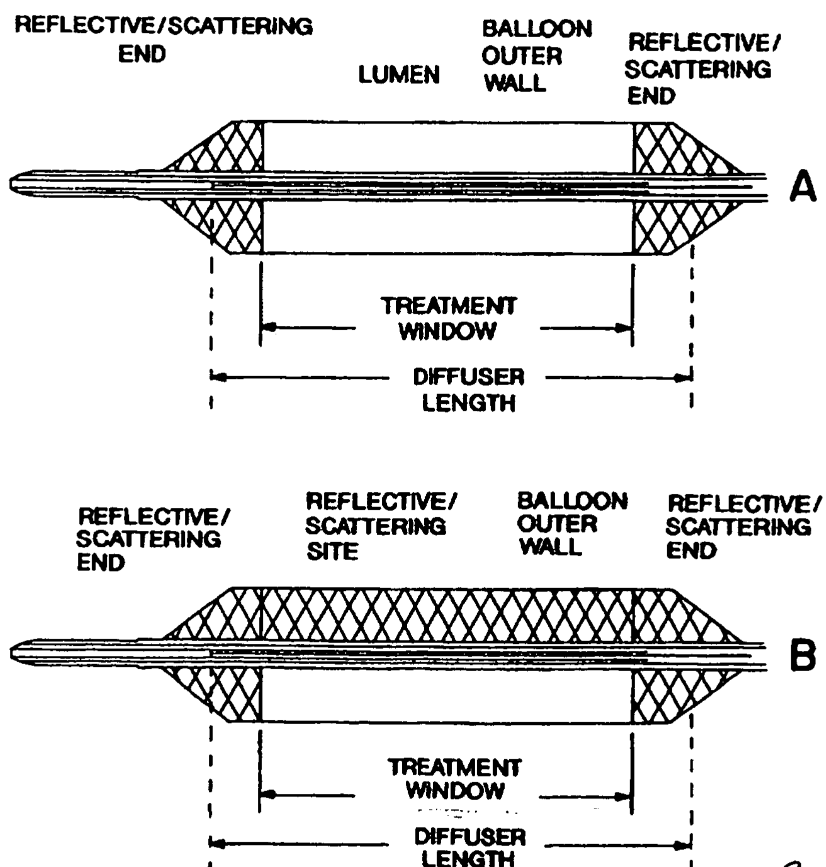
(54) Title: BALLOON CATHETER FOR PHOTODYNAMIC THERAPY

(57) Abstract

The present invention provides improved balloon catheter apparatuses for use in therapies requiring delivery of uniform light to a treatment area. The improved apparatus comprises a balloon having a defined treatment window where the window is delineated using a reflective material. The apparatus may further comprise a fiber optic cable that terminates in a diffusion tip where the diffusion tip is longer than the treatment window. The present invention further provides improved therapeutic methods that use the improved balloon catheters of the present invention.



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BALLOON CATHETER FOR PHOTODYNAMIC THERAPY

Technical Field

The present invention is in the field of medical devices used in administering light to a location within the body of a patient, such as in photodynamic therapy (PDT). The present invention provides improved balloon catheter devices that more evenly distribute light throughout the area of a treatment window.

Background Art

There are a variety of medical procedures that require light or irradiated energy to be administered to a patient within the body. One example is therapeutic methods that use a light activated compound to selectively killing target cells in a patient, termed photoactivated chemotherapy. Other examples include optical diagnostic methods, hypothermia treatment and biostimulation. In photoactivated chemotherapeutic methods, a light-sensitive drug is injected into a patient and a targeted light source is used to selectively activate the light-sensitive drug. When activated by light of a proper wavelength, the light-sensitive drug produces a cytotoxic agent that mediates the destruction of the surrounding cells or tissue.

The main application of photoactivated therapy, such as PDT, is for the destruction of malignant cell masses. Photoactivated therapy has been used effectively in the treatment of a variety of human tumors and precancerous conditions including basal and squamous cells, skin cancers, breast cancer, metastatic to skin, brain tumors, head and neck, stomach, and female genital tract malignancy, cancers and precancerous conditions of the esophagus such as Barrett's esophagus. A review of the

history and progress of photoactivated therapy is provided by Marcus, S. Photodynamic Therapy of Human Cancer: Clinical Status, Potential, and Needs. In Gomer, C.J. (ed.); "Future Directions and Applications in Photodynamic Therapy." Bellingham, W.A. SPIE Optical Engineering Press (1990) pp 5-56 and specific applications of PDT are provided by Overholt *et al.*, *Sem. Surg. Oncol.* *11*:1-5 (1995).

One area of focus in the development of phototherapeutic methods and apparatus is the development of targeted light sources that provide uniform illumination to a given treatment area.

Allardice *et al.* *Gastrointestinal Endoscopy 35*:548-551 (1989) and Rowland *et al.* PCT application WO 90/00914, disclose on type of light delivery systems designed for use with PDT. The disclosed system involves a flexible tube comprising a dilator and a transparent treatment window that defines a treatment area by using opaque end-caps made of stainless steel. A fiber optic element that is connected to a laser and ends in a diffusing tip is used in combination with the dilator to deliver light to a tissue source. Allardice *et al.* discloses that the advantages of this apparatus over the use of balloon-type catheter in providing a more uniform distribution of light.

Nseyo *et al.* *Urology 36*:398-402 (1990) and Lundahl, U.S. Patent Nos. 4,998,930 and 5,125,925, disclose a balloon catheter device for providing uniform irradiation to the inner walls of hollow organs. The device is based on a balloon catheter design and includes a balloon at one end of the apparatus and an optical fiber ending in a diffusion tip that is inserted into the lumen of the balloon through the catheter. The use of the catheter's centering tube was disclosed as providing a more uniform

distribution of the laser light by centering the optical fiber in the inflated balloon. The catheter devices disclosed in these references further incorporate optical sensing fibers in the balloon wall to provide means for measuring illumination. However, there is no disclosure about the use of specific coating materials on the balloon to improve light uniformity or the use of a long diffusion tip that is longer than a delineated treatment window.

Panjehpour *et al. Lasers and Surgery in Medicine 12*:631-638 (1992) discloses the use of a centering balloon catheter to improve esophageal photodynamic therapy. Panjehpour discloses a cylindrical balloon catheter into which a fiber optic probe ending in a light diffuser is inserted. The cylindrical balloon containing the catheter is transparent and is not modified with a reflective coating to improve the diffusion of light within the balloon or to define a treatment window

Overholt *et al. Lasers and Surgery in Medicine 14*:27-33 (1994) discloses modified forms of the balloon catheter device described by Panjehpour. The cylindrical balloon catheter was modified by coating both ends of the balloon with a black opaque coating to define a 360 degree treatment window. Overholt additionally describes a modified balloon in which one-half of the circumference of the treatment window is rendered opaque to light using the black coating material. This configuration provides a 180° treatment window. The black color guard used in the balloon to define the target window was not a reflective material and did not increase the uniformity of the light passing through the treatment window.

Rowland *et al.* PCT application WO 90/00420, discloses a light-delivery system for irradiating a surface. The device comprises a hemispherical shell

whose inside is entirely coated with a diffuse reflector and a light source that is mounted within the shell. The light source may contain a diffusing source at the tip allowing diffusion of light within the reflective shell.

Spears, U.S. Patent No. 5,344,419, discloses apparatuses and methods for making laser-balloon catheters. Spears utilizes a process that etches an end of a fiber optic cable to provide a diffusion tip on the optical cable. The optical cable containing the etched tip is secured within a central channel of a balloon catheter using a coating of adhesive containing microballoons. The position of the tip within the central channel and the microballoons contained in the adhesive provide increased efficiency in diffusing the laser radiation in a cylindrical pattern, providing a more uniform illumination at the target site.

Beyer, *et al.* U.S. Patent No. 5,354,293 discloses a balloon catheter apparatus for delivering light for use in PDT. The balloon catheter device disclosed employs a conical tipped fiber optic cable to provide means of deflecting a light beam radially outward through a transparent portion of an inflated catheter.

In summary, there have been numerous devices that have been developed for use in PDT that employ a balloon catheter to support a light source in an ideal central point within a target area that is to be illuminated (Spears, Overholt, Beyer, Lundahl and Allardice) The main benefits of using a centering type balloon are that 1) the clinician does not have to hold the fiber optic in the central location, this is done automatically by the balloon catheter, 2) the light dose is more uniform across the entire treatment are than would be the case of light delivered by a fiber optic that is held central to the treatment volume without the aid of a balloon (while

this is true with existing designs of balloon catheters, it is herein demonstrated that the uniformity can be significantly improved), 3) the treatment field is kept clean of contaminants e.g. blood, urine that might absorb the light and so effect the final PDT result, and 4) the overall treatment procedure can be considerably shortened as it is simpler setting up the fiber optic and getting the light dose correct. However, the disadvantage of using current cylindrical centering balloons with existing fiber optic diffusers is the inability to obtain uniform light being transmitted through the balloon to the target site.

Although each of the above disclosures provides means for providing light to a target site, there is no suggestion to use a reflective coating at the ends of a balloon catheter as a means of increasing uniformity in the distribution of the transmitted light. In addition, none of the devices employs a diffusing tip at the end of the fiber optic cable that is longer than the treatment window. These two features are present, alone or in combination, in the apparatus of the present invention and provides improved balloon catheter devices that more uniformly and efficiently distribute light over a treatment area.

Summary of the Invention

The present invention provides improved balloon catheter apparatuses for use in therapeutic methods that require light illumination to a specific site. The improved apparatus comprises a balloon having a defined treatment window where the window is delineated using material that reflects and/or scatters light back towards the lumen of the balloon and zone defined as the treatment window. The apparatus may further comprise a fiber optic cable that terminates in a diffusion tip

where the diffusion tip is longer than the treatment window.

The present invention further provides improved phototherapeutic methods that use the improved balloon catheters of the present invention.

Brief Description of the Drawings

Figure 1 provides a diagrammatic representation of the balloon components of the apparatus of the present invention. Panel A shows a balloon that provides a 360 degree treatment window. Panel B shows a balloon that provides a treatment window that is not 360 degrees.

Figure 2 shows scans of non-reflective, black-end coated catheters (Overholt catheter) having a 30mm window using a fiber optic cable ending in a 25mm diffuser, with and without white paper to simulate the effect of tissue scattering.

Figure 3 shows scans of non-reflective, black-end coated catheters (Overholt catheter) having a 30mm window using a fiber optic cable ending in a 30mm diffuser, with and without white paper to simulate the effect of tissue scattering.

Figure 4 shows scans of non-reflective, black-end coated catheters (Overholt catheter) having a 30mm window using a fiber optic cable ending in a 50mm diffuser, with and without white paper to simulate the effect of tissue scattering.

Figure 5 shows scans of reflective, white-end coated catheters having a 30mm window using a fiber optic cable ending in a 25mm diffuser, with and without white paper to simulate the effect of tissue scattering.

Figure 6 shows scans of reflective, white-end coated catheters having a 30mm window using a fiber optic cable ending in a 30mm diffuser, with and without white paper to simulate the effect of tissue scattering.

Figure 7 shows scans of reflective, white-end coated catheters having a 30mm window using a fiber optic cable ending in a 50mm diffuser, with and without white paper to simulate the effect of tissue scattering.

Figure 8 shows scans of non-reflective, black-end coated catheters having a 50mm window using a fiber optic cable ending in a 50mm diffuser, with and without various colored paper to simulate the effect of tissue scattering.

Figure 9 shows scans of non-reflective, black-end coated catheters having a 50mm window using a fiber optic cable ending in a 70mm diffuser, with and without various colored paper to simulate the effect of tissue scattering.

Figure 10 shows scans of reflective, white-end coated catheters having a 50mm window using a fiber optic cable ending in a 50mm diffuser, with and without various colored paper to simulate the effect of tissue scattering.

Figure 11 shows scans of reflective, white-end coated catheters having a 50mm window using a fiber optic cable ending in a 70mm diffuser, with and without various colored paper to simulate the effect of tissue scattering.

Figure 12 shows scans of non-reflective, black-end coated catheters having a 70mm window using a fiber optic cable ending in a 50mm diffuser, with and without white colored paper to simulate the effect of tissue scattering.

Figure 13 shows scans of non-reflective, black-end coated catheters having a 70mm window using a fiber optic cable ending in a 70mm diffuser, with and without white colored paper to simulate the effect of tissue scattering.

Figure 14 shows scans of reflective, white-end coated catheters having a 70mm window using a fiber optic cable ending in a 50mm diffuser, with and without white colored paper to simulate the effect of tissue scattering.

Figure 15 shows scans of reflective, white-end coated catheters having a 70mm window using a fiber optic cable ending in a 70mm diffuser, with and without white colored paper to simulate the effect of tissue scattering.

Figure 16 shows scans of reflective coated catheters in which the length of the fiber active region and the balloon window are equivalent.

Figure 17 shows scans of reflective coated catheters in which the length of the fiber active region is 2 cm longer than the balloon window.

Detailed Description of the Invention

The present invention provides improved balloon catheter devices for providing light irradiation to a defined area. Previous art-known balloon catheters, such as those disclosed by Overholt *et al. Lasers and Surgery in Medicine 14*:27-33 (1994), utilize an absorbing coating, such as black Color Guard supplied by Permatex Industrial Corp. Avon, CT, on portions of the balloon to prevent the light from being transmitted through portions of the balloon. The non-blacked-out portions of the balloon thus define a treatment window that can be 360 degrees or can be segmented to be less than the entire circumference of the balloon, for example a 180 degree treatment window. It has been found that the intensity and overall uniformity of the light transmitted through the treatment window can be dramatically increased by using a coating that reflects and/or scatters light into

the lumen of the balloon rather than the black absorbing coating used in the Overholt catheter.

Additionally, previously disclosed balloon catheter devices used in phototherapeutic methods employ a fiber optic cable ending in a diffusion tip that is centered in the balloon to provide even radial distribution of the light transmitted through the cable. The present invention improves on this configuration by disclosing that the intensity and overall uniformity of light transmitted through the treatment window can be increased by employing a diffusion tip that is longer than the treatment window.

Utilizing these observations, the present invention provides improved balloon catheters for use in providing light irradiation to a defined area. As used herein, light irradiation, light or irradiation, refers to light of wavelengths from about 300nm to about 1200nm. This includes UV, visible and infrared light. The choice of wavelength will be based on the intended use, namely being selected to match the activation wavelength of the photoactivated drug or the wavelength used for irradiation when a photoactivated compound is not employed. Examples of photoactivated compounds include, but are not limited to ALA, SnET2, phthalocyanines, BPD, PHOTOFRIN, MACE, psoralen, and derivatives thereof.

In one embodiment, the apparatus comprises an optically clear central channel into which a fiber optic probe can be inserted and an outer sleeve having a proximal end and a distal end and containing an inflatable balloon proximal to the distal end.

The balloon portion of the apparatus of the present invention can be manufactured to be any of a variety of shapes when inflated. Such shapes include, but are not limited to, spherical and cylindrical shapes with tapering ends. The preferred shape will depend on the

shape and nature of the area of treatment. For example, when treating the esophageal tract, e.g., when treating Barrett's esophagus, a cylindrical shape with tapering ends is preferred.

The size and shape of the balloon and treatment will depend on the intended use. For example, when the device of the present invention is used to treat Barrett's esophagus, the preferred shape is cylindrical and will be from about 10mm to about 200mm in length and from about 10mm to 35mm in diameter when inflated. The diameter being selected to flatten the folds in the esophagus.

Any semi-resilient material that can form a balloon that can be inflated using either air or fluid can be used in making the balloon component of the present apparatus. The material can be either transparent or translucent. The preferred material will be transparent and non-distendable. The preferred material is a polyurethane membrane of a thickness of about 0.11 mm. However, any material that is used in the construction of other art known inflatable balloon catheters can readily be used in the devices of the present invention.

The balloon used in this embodiment of the apparatus of the present invention contains a reflective material that reflects and preferably also scatters light into the lumen and treatment window of the balloon. The material is contained on the ends of the balloon and the area that is not coated with the reflecting material defines a treatment area or window.

As used herein, a material is said to be reflective if the material prevents the transmission of light through the material by deflecting the light striking the material. The preferred material will also be able to scatter the deflected light, providing a diffuse reflection of the light hitting the material. The function of the reflective material is to provide

increased uniformity and efficiency in the light transmitted through the treatment window and to prevent light from exposing non-target areas outside the treatment window.

Figure 1 provides a diagrammatic representation of a balloon catheter that contain a reflective coating at both ends (panel a), or a reflective coating at both ends and a reflective coating over a portion of the circumference of the treatment window of the balloon (panel b).

Any coating material that is reflective, and in addition, can preferably scatter the reflected light, can be used as the reflective coating for the balloon component of this embodiment of the apparatus of the present invention. Examples of coating material include, but are not limited to, titanium dioxide, aluminum, gold, silver, and dielectric films. The choice of reflective material used will depend, in a large part, on the material used in the balloon, the method used to manufacture the balloon and the wavelength of light used in the phototherapy. A skilled artisan can readily adapt known reflective materials for incorporation into the balloon component of the apparatus of the present invention.

The preferred reflective material will reflect and scatter light and prevent from about 20% to 100% of light striking the material from passing through the material. The most preferred will reflect and scatter from about 70% to about 100% of the light.

The reflective material can be incorporated in the balloon component of the apparatus of the present invention in a variety of ways. For example, the reflective material can be applied to the surface of the balloon after the balloon is formed, for example by using a dipping process. Alternatively, the reflective

material can be directly incorporated into the material used to form the balloon during the manufacturing of the balloon. The method used to incorporate the reflective material into the balloon will be based primarily on the reflective material used, the material the balloon is made of, and the method used to manufacture the balloon component. A skilled artisan can readily employ art-known procedures for incorporating a reflective material within or onto a surface of a balloon.

In addition to a reflective coating, the balloon component may further have an additional opaque coating over the reflective coating. An opaque coating is used to further prevent light from exiting the balloon outside the defined treatment window.

The balloon component may further contain optical sensors. Optical sensors that are integral to the balloon component can be used to measure the intensity of illumination when the catheter is used therapeutically. Optical sensors, such as a fiber optic probe or a photodiode as part of a balloon catheter, have been described in US Patent No. 5,125,925.

The apparatus of the present invention may further comprise a fiber optic cable, a fiber optic bundle or liquid light guide, for convenience, hereinafter referred collectively as a fiber optic cable. The fiber optic cable will contain one end that is readily attachable to a laser or non-laser light source and a second end onto which a diffuser is attached.

The light carrying section of the fiber optic cable, hereinafter the fiber optic core, can be of any diameter so long as the fiber optic cable can be inserted into the central channel of the balloon catheter. The preferred fiber optic core will be from about 50 to about 1000 microns in diameter, preferably about 400 microns. The choice of the core diameter will depend on the brightness

of the light source and the optical power output required from the fiber optic diffuser tip.

As stated above, the fiber optic cable will terminate in a diffusion tip or diffuser. As used herein, a diffuser or diffusion tip, is defined as an element that can be attached to the end of a fiber optic cable, or a structure that can be formed at the end of the fiber optic cable, that provides a means for diffusing (scattering) the light being transmitted through the fiber optic cable so that it radiates outward from the fiber. Fiber optic diffusers are readily available and can be created by a variety of methods including, but not limited to, surrounding a central core with a scattering media or a scattering film, tapering the tip of the fiber optic cable to form a conical tip, or by inserting a tapered fiber optic tip into a cylindrical body containing optical scattering media. A variety of diffusion tips for using in PDT apparatus are described in U.S. Patent Nos. 5,431,647, 5,269,777, 4,660,925, 5,074,632, and 5,303,324. The preferred diffusing tip for the fiber optic cable contained in the apparatus of the present invention is the cylindrical diffusion tip described in SBIR application grant 2R44CA60225/02 and are available from Laserscope (CA).

The length of the diffusion tip can be varied relative to the size of the treatment window defined by the reflective material at the ends of the balloon component. It has been found that the intensity and uniformity of light being transmitted through the treatment window can be optimized by selecting a diffusion tip that is longer than the treatment window. additionally, the longer diffusion tip eliminates the need for precise positioning of the fiber optic in the center of the treatment window In the Examples that follow, it was found that a diffusion tip that is longer

than the treatment window provided an increase in the uniformity of light being transmitted through the treatment window. Preferably, the diffusion tip will extend from about 0.3cm to about 5cm on either side of the treatment window.

Recent developments in producing small efficient light emitting diodes (LEDs) permits the use of a probe having multiple LEDs mounted on an end to form a distributed array. Such a probe can replace the fiber optic cable and diffuser by being inserted, LED end first, into the central channel. The LEDs emit a diverging beam of light without the need for a diffuser, although a diffuser can be incorporated into such a probe to increase diffusion. In such a configuration, the LEDs cover the probe to a length equivalent to the diffuser tip and is equivalent to, and referred to as the fiber optic cable or probe.

In an alternative configuration, the balloon component can be provided without the optically clear central channel. In such a configuration, a fiber optic cable containing the diffusion tip is connected to the distal end of the balloon and is pulled to a central location when the balloon is inflated.

The catheters of the present invention can be used with any wavelength of light. The choice of the wavelength will be determined by the intended use. In the examples that follows, 633nm wavelength light, supplied using a helium neon laser, was used. This is the activation wavelength for a variety of photoactivated compounds used in PDT. The choice of materials used in each of the components of the catheters of the present invention, and in particular the reflective coating and the overall geometry of the finished assembly, can be specifically tailored to provide the desired properties

for a given treatment wavelength and indication being treated.

Each component of the improved balloon catheters of the present invention, namely the reflective coating and a diffusion tip that is longer than the treatment window, provides increased uniformity and efficiency in transmitting light to a defined treatment area. Each component can be used independently with presently available catheters, for example a longer tip can be used with an Overholt style catheter, or both components can be used in combination.

The present invention further provides improved methods for irradiating a surface with light. Specifically, the improved methods rely on the use of the balloon catheters of the present invention. The balloon catheters of the present invention are particularly useful in PDT for the treatment of malignancies of the esophagus, particularly Barrett's esophagus, for biostimulation and the treatment of hypothermia. The devices of the present invention can readily be used by a skilled artisan in all known phototherapeutic and illumination applications for which a balloon illumination catheter can be used.

The following examples are intended to illustrate but not to limit the invention. All of the cited references are herein incorporated by reference.

Example 1

The following data provides a comparison of the present disclosed balloon catheters and balloon catheters essentially as described by Overholt *et al. Lasers and Surgery in Medicine 14*:27-33 (1994). The data summarizes studies performed using balloons with black ends (B) or

reflective white ends (W) under condition with and without a simulated tissue reflector at the wall of the balloon (referred to either paper:none or paper:white). Additionally, a comparison of different balloon window length/fiber optic diffuser lengths is provided.

Data was collected using an automated scanning system that utilizes a modified UDT photodiode (Grasaby Optronics (FL)) as a detector essentially as described by Kozodoy, *et al.*, *"New system for Characterising the Light Distribution of Optical Fiber Diffusers for PDT Application" Proc. SPIE OE/LASE* 2131A-16 (Jan. 1994) and modified to collect linear scans for the purposes of these tests. Light of 633nm wavelength was provided to the fiber optic probe using a helium neon laser (Aerotech, PA). The balloon catheters were supplied by Polymer Technology Group (CA). The optical diffuser tips were supplied by Laserscope (CA).

The data in this example was obtained by simulating a reflective end capped balloon by painting white liquid paper (Gillette (MA)) on the ends of a transparent PTG balloon. The data presented in Examples 2 and 3 used balloon catheters containing a reflective TiO_2 coating that were specifically manufactured by PTG.

Figures 2-15 summarizes the data collected. Each figure shows one or more scans along the length of the balloon window for a variety of different parameters. The figures show the normalized light intensity/fluence rate (y-axis) plotted against the position along the balloon window (x-axis). All of the figures are plotted so that the y-axis from one figure to the other can be directly compared. The x-axis matches the balloon catheter window length (X=0 is the center of the treatment window).

As can be seen, the light intensity drops off as the detector starts to intersect the edges of the window ("window edge effect" zone). The point at which the intensity drops off in this zone is determined by the finite diameter of the detector (2 mm in this case). The 2 mm diameter factors in the averaging of light in tissue that results from scattering. For the purpose of analyzing the data and comparing it from one geometry to another, the section of the scan beyond the areas labeled as the "window edge effect" was ignored and only the central section of the scans were utilized. Each scan also has shown alongside it the average intensity, and the caption at the bottom identifies the parameters being investigated.

The figures can be split into 3 broad groups: Figures 2-7 show all the 30 mm balloon window data; Figures 8-11 show all the 50 mm balloon window data; Figures 12-15 show all the 70 mm balloon window data.

Tables 1 and 2 summarize the numbers that have been compiled from the data presented in Figures 2-15. Table 1 provides the data obtained with a fiber optic diffuser that matches the length of the balloon window while Table 2 provides the data obtained with a fiber optic diffuser that is 2 cm longer than the balloon window.

In addition to the basic description of the parameters being used and the average and standard deviation, both tables provide calculated values for the "goodness of uniformity". This is defined as the percentage of the scan length within a defined plus/minus band from the mean. A number of plus/minus tolerances (+ 10%, + 20%, + 30%) were deliberately chosen to see what impact this would have on the values calculated. The region that were of particular interest is the "Properly Treated Region" (PTR), and values approaching 1.0 were considered as being excellent (all power within tolerance

limits), and numbers less than this having some power outside of the tolerances. PTR is meant to refer to whether the light with a local intensity within this tolerance will produce the desired PDT response in tissue.

One of the difficulties facing the development of effective PDT for treating disorders of the esophagus is that there is little information of how critical the light uniformity needs to be in phototherapeutic methods such as PDT treatment of Barrett's esophagus. However, it is reasonable to conclude that increased uniformity of transmitted light should yield a more even response in the treated area, potentially avoiding the need to retreat an given region. Based on the above, using the ±10% data in Tables 1 and 2 as the data that is used to determine the ideal balloon catheter and fiber optic geometry, with a nominal acceptance criteria of >0.70 as being a good value for the PTR, then the fiber optic balloon catheter configurations that meet typical clinical needs will 1) have a fiber optic diffusion tip that is approximately 2 cm longer than the treatment window and 2) will have reflecting end material that defines the limits of the treatment window.

An additional important characteristic relates to the average value of the intensity (I_{av}) for each balloon catheter/ fiber optic combination measured at the balloon window. With reflective coated, white-end catheters and white paper around the balloon to simulate tissue scattering: a 3cm window and 5cm diffuser had a I_{av}=3.6; a 5cm window and 5cm diffuser had a I_{av}=3.5; a 7cm window and 7cm diffuser had a I_{av}=3.5; a 3cm window and 5 cm diffuser had a I_{av}=3.6; and a 5cm window and 7cm diffuser had a I_{av}=4.0.

With no paper around the balloon to simulate tissue scattering: a 3cm window and 5cm diffuser had a I_{av}=1.8; a

5cm window and 5cm diffuser had a I_{av}=1.3; a 7cm window and 7cm diffuser had a I_{av}=1.3; a 3cm window and 5cm diffuser had a I_{av}=1.8; and a 5cm window and 7cm diffuser had a I_{av}=1.3.

For all the data given above, the power output from each length of fiber optic diffuser was normalized to a single power/cm output from the diffuser tip P, (mW/cm) so the I_{av} data from the various combinations given above can be directly compared.

Within each data set (white paper vs. no white paper) the average values of I_{av} are reasonably similar (to within $\pm$10-20% of their mean). This implies that a single J/cm value can be set for each fiber optic, i.e., the clinician measures the power required according to a known mW/cm for each fiber optic.

The I_{av} obtained for non-reflective, black-end coated catheters, using white paper to simulate tissue scattering: a 3cm window and 2.5cm diffuser had a I_{av}=1.1; and a 5cm window and 5cm diffuser had a I_{av}=2.1. With no paper to simulate tissue reflection: a 3cm window and 2.5cm diffuser had a I_{av}=0.7; and a 5cm window and 5cm diffuser had a I_{av}=1.0. (See Table 2).

Clinically, Overholt has found it necessary to use 250-300 J/cm for the 3 cm balloon and 125-150 J/cm for the 5 cm balloon (____). Overholt's light doses define a ratio of 1.67-2.4:1 (average of 2:1) for the different balloon catheters combinations he used. This is comparable to the values measured above by looking at ration calculated with and without white scattering paper, i.e., 1.4-2.0:1.

Another key point to note is that the average intensity measure above with the various geometry's are higher than those obtained using an Overholt catheter. This means, quite significantly, that where Overholt is

using a light dose of about 275 J/cm with his 3 cm balloon, the present catheter would use only

$$275 \times (1.1/3.6) = 84 \text{ J/cm}$$

to get the same clinical result and the same light dose (J/cm^2) at the tissue with any of the disclosed balloon lengths. This can be used as a benefit in two ways. With existing balloon catheters (black ended) 400mW/cm is typically used, resulting in a treatment time of 11.5 minutes for 275 J/cm. With the reflective end balloon and diffuser tip that is longer than the treatment window, either the treatment time can be reduced (for example to 7 minutes at 200 mW/cm) or the mW/cm can be reduced to 84 mW/cm. The latter is extremely important since it would allow the use of inexpensive laser diodes, even when using a 9cm diffuser (1.1 W laser diode needed assuming a 30% loss in the fiber optic).

Based on the above results, a balloon with white ends provides a more uniform light dose at tissue, and this together with an appropriate cylindrical diffuser length fiber optic will permit a single Pl (mW/cm) and El (J/cm) to be used for PDT treatment with all such balloon catheter/fiber optic combinations. An additional benefit is that the integration effect produced by the reflecting balloon ends allows for the reduction in the treatment time or the ability to use less expensive, lower power lasers.

In summary, extensive testing has shown that quite unexpectedly, by changing the ends of the Overholt Barrett's style balloon catheter from a black absorbing material to reflecting/scattering material, together with the use of fiber optics that overlap the treatment window, the uniformity of the light at the balloon surface is significantly improved. Prior to the present investigation of the optical characteristics of balloon

catheters, it was assumed that opaque balloon catheter ends should be used simply to prevent the light from passing beyond the ideal treatment zone and it was believed that the light dosimetry would be similar for each balloon catheter irrespective of length. Recently Overholt and Panjehpour have collected clinical data that confirms the assumption that with a black ended balloon catheter, a single light dose EL cannot be used (____).

When the light field out of the balloon catheter with black ends was measured, it was observed that the light was decaying as the edges of the windows were approached, and so the black balloon ends were changed to a reflecting material. An improvement in the uniformity profile was observed, although the uniformity still dropped off at the ends. When the fiber optic diffuser was extended beyond the window length, a further improvement in the uniformity profile was observed. Using this configuration, it was possible to define a balloon catheter/fiber optic geometry that allows a single value of EL to be defined.

An additional surprising benefit was that the integration effect obtained with the catheters of the present invention is sufficiently great that low power lasers may now be usable in areas that were previously impossible. This opens up many opportunities for PDT as the need for costly high power lasers has been a significant limitation. In particular it is likely that laser diodes with a 1.5W output and operating at 630nm will now be usable to treat Barrett's esophagus, even though the currently planned treatment lengths are up to 7cm long. Previously this would have been unthinkable as a means for delivering the light dose required for typical PDT methods since the treatment time would need to be about 1 hour using 3 to 4 treatment segments to cover the entire 7cm length.

Example 2

The following data was generated using reflective coated, TiO_2, white-ended balloons (provided by the Polymer Technology Group).

The results are presented in Table 3. The data has been normalized in such a way that it can be directly compared with the data provided in the previous examples.

Focusing on the scans generating using white paper to simulate tissue scattering of the administered light, the key factors to notice are:

1. The result confirm the results obtained in Example 1 using a balloon that incorporates a clinically viable scatter in the wall, namely TiO_2.

2. The mean average is roughly constant (4.34 to 4.44; a difference of only a few percent). Previously, the uncertainty about the variability in the integration factor was a cause for concern. The integration constant is also higher than for previous measurements (the ends have higher reflectivity).

3. The properly treated region (PTR) remains high--no less than 88.7%.

4. The coefficient of variation is low and roughly constant (the standard deviation is no greater than 7% of the mean).

This demonstrates that with a well thought out design, matching the reflectivity of the white ended balloons to the lengths, the mean average can be held constant irrespective of the balloon window length. The higher integration factor will help reduce the requirements of the light system used to deliver light to the fiber optic.

Example 3

Figures 16 and 17 provide graphical scans that can be used to compare the uniformity of light through the treatment window obtained with different window size/diffuser size combinations. Figure 16 shows the scans for cases in which the lengths of the diffuser and the balloon window are equivalent. Figure 17 shows the scans for cases in which the length of the diffuser is 2 cm longer than the balloon window. Both scans were performed in the presence of a white scatter paper to simulate tissue scattering effects.

The data present in Figures 15 and 16 are summarized in Table 3. Table 3 further contains a summary of results obtained when a white scatter paper was not used.

These result provided confirms and further supports the conclusions provided in Example 3, namely the advantages of using the longer fiber optics and a reflective coating.

Table 1

	T1	T2	T9	T10	T21	T22	T33	T34	T41	T42	T45	T46
Paper	None	White	None	White	None	White	None	White	None	White	None	White
Ends	B	B	W	W	B	B	W	W	B	B	W	W
Diffuser	5	5	5	5	3	3	3	3	7	7	7	7
Balloon	5	5	5	5	3	3	3	3	7	7	7	7
Mean Average	1.000	2.149	1.295	3.494	0.839	1.290	1.121	2.161	1.116	2.272	1.347	3.463
Standard Deviation	0.147	0.362	0.133	0.291	0.099	0.187	0.146	0.279	0.146	0.391	0.098	0.314
Coefficient of Variation	0.147	0.169	0.103	0.083	0.118	0.145	0.130	0.129	0.130	0.172	0.073	0.091
Max (as Prcnt of Mean)	1.160	1.227	1.107	1.117	1.136	1.179	1.128	1.137	1.134	1.204	1.082	1.112
Min (as Prcnt of Mean)	0.635	0.536	0.674	0.640	0.712	0.637	0.649	0.610	0.634	0.536	0.670	0.668
** +/-30% **												
Undertreated Region	0.041	0.073	0.007	0.011	0.000	0.042	0.032	0.032	0.022	0.072	0.004	0.007
Overtreated Region	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Properly Treated Region	0.959	0.927	0.993	0.989	1.000	0.958	0.968	0.968	0.978	0.928	0.996	0.993
** +/-20% **												
Undertreated Region	0.136	0.170	0.057	0.045	0.085	0.132	0.111	0.106	0.112	0.162	0.022	0.039
Overtreated Region	0.000	0.050	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.011	0.000	0.000
Properly Treated Region	0.864	0.780	0.943	0.955	0.915	0.868	0.889	0.894	0.888	0.827	0.978	0.961
** +/-10% **												
Undertreated Region	0.261	0.247	0.181	0.109	0.222	0.238	0.222	0.206	0.235	0.283	0.077	0.173
Overtreated Region	0.367	0.429	0.073	0.043	0.270	0.291	0.317	0.323	0.325	0.364	0.000	0.042
Properly Treated Region	0.372	0.324	0.746	0.848	0.508	0.471	0.460	0.471	0.441	0.353	0.923	0.785

Table 2

	T5	T6	T13	T14	T17	T18	T25	T26	T29	T30	T37	T38
Paper	None	White	None	White	None	White	None	White	None	White	None	White
Ends	B	B	W	W	B	B	B	B	W	W	W	W
Diffuser	7	7	7	7	2.5	2.5	5	5	2.5	2.5	5	5
Balloon	5	5	5	5	3	3	3	3	3	3	3	3
Mean Average	0.98	2.26	1.30	3.98	0.69	1.08	1.15	1.75	0.91	1.81	1.84	3.61
Standard Deviation	0.05	0.25	0.09	0.16	0.10	0.18	0.10	0.21	0.13	0.25	0.16	0.29
Coefficient of Variation	0.05	0.11	0.07	0.04	0.15	0.17	0.09	0.12	0.14	0.14	0.08	0.08
Max (as Prcnt of Mean)	1.05	1.15	1.14	1.07	1.17	1.21	1.09	1.12	1.14	1.15	1.09	1.09
Min (as Prcnt of Mean)	0.82	0.66	0.71	0.83	0.62	0.58	0.73	0.65	0.61	0.59	0.67	0.70
** +/-30% **												
Undertreated Region	0.00	0.02	0.00	0.00	0.05	0.07	0.00	0.03	0.05	0.04	0.01	0.01
Overtreated Region	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Properly Treated Region	1.00	0.98	1.00	1.00	0.95	0.93	1.00	0.97	0.95	0.96	0.99	0.99
** +/-20% **												
Undertreated Region	0.00	0.08	0.01	0.00	0.12	0.16	0.04	0.10	0.12	0.12	0.05	0.04
Overtreated Region	0.00	0.00	0.00	0.00	0.00	0.07	0.00	0.00	0.00	0.00	0.00	0.00
Properly Treated Region	1.00	0.92	0.99	1.00	0.88	0.76	0.96	0.90	0.88	0.88	0.95	0.96
** +/-10% **												
Undertreated Region	0.06	0.18	0.02	0.02	0.26	0.28	0.16	0.21	0.23	0.22	0.12	0.12
Overtreated Region	0.00	0.16	0.09	0.00	0.36	0.38	0.00	0.19	0.35	0.29	0.00	0.00
Properly Treated Region	0.94	0.66	0.89	0.98	0.38	0.35	0.84	0.60	0.41	0.49	0.88	0.88

Table 3

New Data Using PTG Double-thickness White-Ended Balloons (25% TIO2 Loading)

File Name	53WE	75WE	97WE	53NE	75NE	97NE	33WE	55WE	77WE	33NE	55NE	77NE
Fiber Length (cm)	5	7	9	5	7	9	3	5	7	3	5	7
Balloon Length (cm)	3	5	7	3	5	7	3	5	7	3	5	7
Scattering Paper	White	White	White	None	None	None	White	White	White	None	None	None
Mean Average	4.44	4.34	4.37	1.74	1.50	1.35	2.99	3.70	3.85	1.17	1.26	1.20
Standard Deviation	0.16	0.31	0.23	0.11	0.21	0.17	0.27	0.33	0.26	0.09	0.11	0.19
Coefficient of Variation	0.04	0.07	0.05	0.06	0.14	0.13	0.09	0.09	0.07	0.07	0.09	0.16
Max (as Prcnt of Mean)	107.9%	113.1%	109.9%	111.3%	130.3%	132.6%	113.8%	113.7%	113.1%	106.4%	110.7%	136.1%
Min (as Prcnt of Mean)	93.0%	70.6%	78.4%	73.9%	53.0%	52.3%	72.2%	66.6%	68.8%	67.5%	58.7%	63.8%
** +/-10% **												
Undertreated Region	0.0%	6.2%	3.6%	3.5%	23.7%	3.6%	10.5%	13.4%	5.8%	8.8%	7.2%	33.6%
Overtreated Region	0.0%	5.2%	0.0%	7.0%	23.7%	16.8%	15.8%	8.2%	4.4%	0.0%	3.1%	24.1%
Properly Treated Region	100.0%	88.7%	96.4%	89.5%	52.6%	79.6%	73.7%	78.4%	89.8%	91.2%	89.7%	42.3%

Claims

1. An apparatus for providing irradiation to a defined area, said apparatus comprising a balloon catheter having a defined treatment window comprising:

i) a clear central channel into which a fiber optic probe can be inserted; and

ii) an outer sleeve, for use in inflating a balloon, having a proximal end and a distal end, said sleeve further containing an inflatable balloon proximate to said distal end; wherein said balloon is coated on both ends with a reflective material so as to define a treatment window.

2. The apparatus of claim 2, wherein said treatment window is from about 1 cm to 20 cm in length.

3. The apparatus of claim 1 wherein the treatment window in said balloon is cylindrical in shape.

4. The apparatus of claim 3 wherein said cylindrical treatment window is from about 3mm to about 200mm in length and from about 1mm to 100mm in diameter when inflated.

5. The apparatus of claim 1 wherein said reflective coating is selected from the group consisting of TiO_2, aluminum, silver or gold.

6. The apparatus of claim 1 further comprising a fiber optic cable that terminates in a diffuser, said diffuser being longer than said treatment window.

7. The apparatus of claim 6, wherein said diffuser is a cylindrical diffuser.

8. The apparatus of claim 7 wherein said diffuser is about 2 cm longer than said treatment window.

9. The apparatus of claim 1 wherein said balloon is made of high density polyurethane.

10. The apparatus of claim 1 wherein said treatment window is transparent.

11. The apparatus of claim 1 wherein said treatment window is translucent.

12. The apparatus of claim 1 further comprising one or more optical sensor attached to the wall of said balloon.

13. An improved balloon catheter apparatus containing a defined treatment window for providing irradiation to a defined area, said improvement comprising using a reflective material to define the treatment window.

14. An improved balloon catheter apparatus containing a defined treatment window for providing irradiation to a defined area, said improvement comprising a fiber optic diffusion tip that is longer than said treatment window.

15. An improved balloon catheter apparatus containing a defined treatment window for providing irradiation to a defined area, said improvements comprising using a reflective material to define the treatment window and a fiber optic diffusion tip that is longer than said treatment window.

16. An improved method for administering light to a defined target area or for use with photodynamic therapy (PDT) said improvement comprising the use of a balloon catheter as defined in claim 1.

17. The method of claim 16, wherein a laser diode of less than about 1.5W is used as a laser light source.

18. An improved method for administering light to a defined target area or for use with photodynamic therapy (PDT) said improvement comprising the use of a balloon catheter as defined in claim 6.

19. The method of claim 18, wherein a laser diode of less than about 1.5W is used as a laser light source.

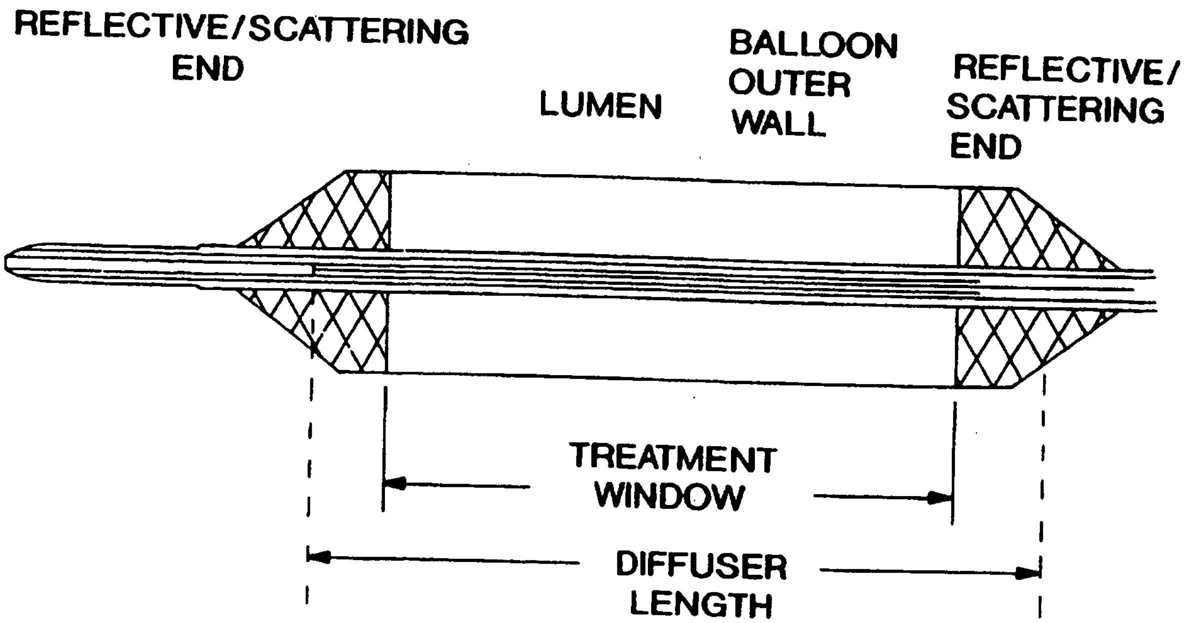

REFLECTIVE/SCATTERING END
LUMEN
BALLOON OUTER WALL
REFLECTIVE/ SCATTERING END
TREATMENT WINDOW
DIFFUSER LENGTH

FIG. 1A

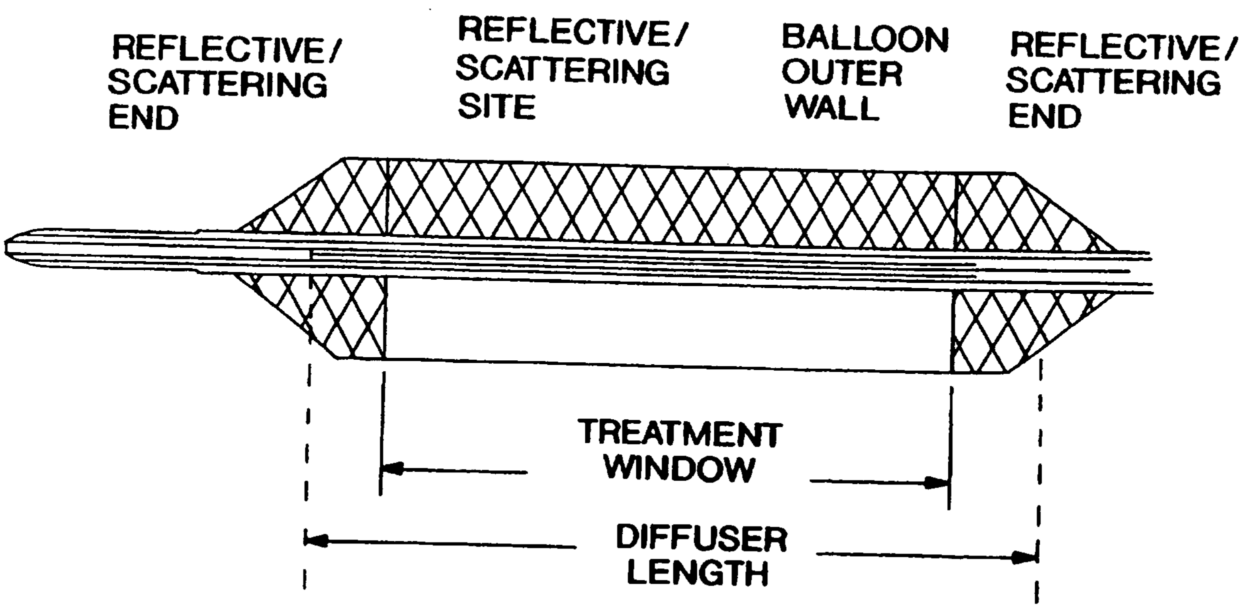

REFLECTIVE/ SCATTERING END
REFLECTIVE/ SCATTERING SITE
BALLOON OUTER WALL
REFLECTIVE/ SCATTERING END
TREATMENT WINDOW
DIFFUSER LENGTH

FIG. 1B

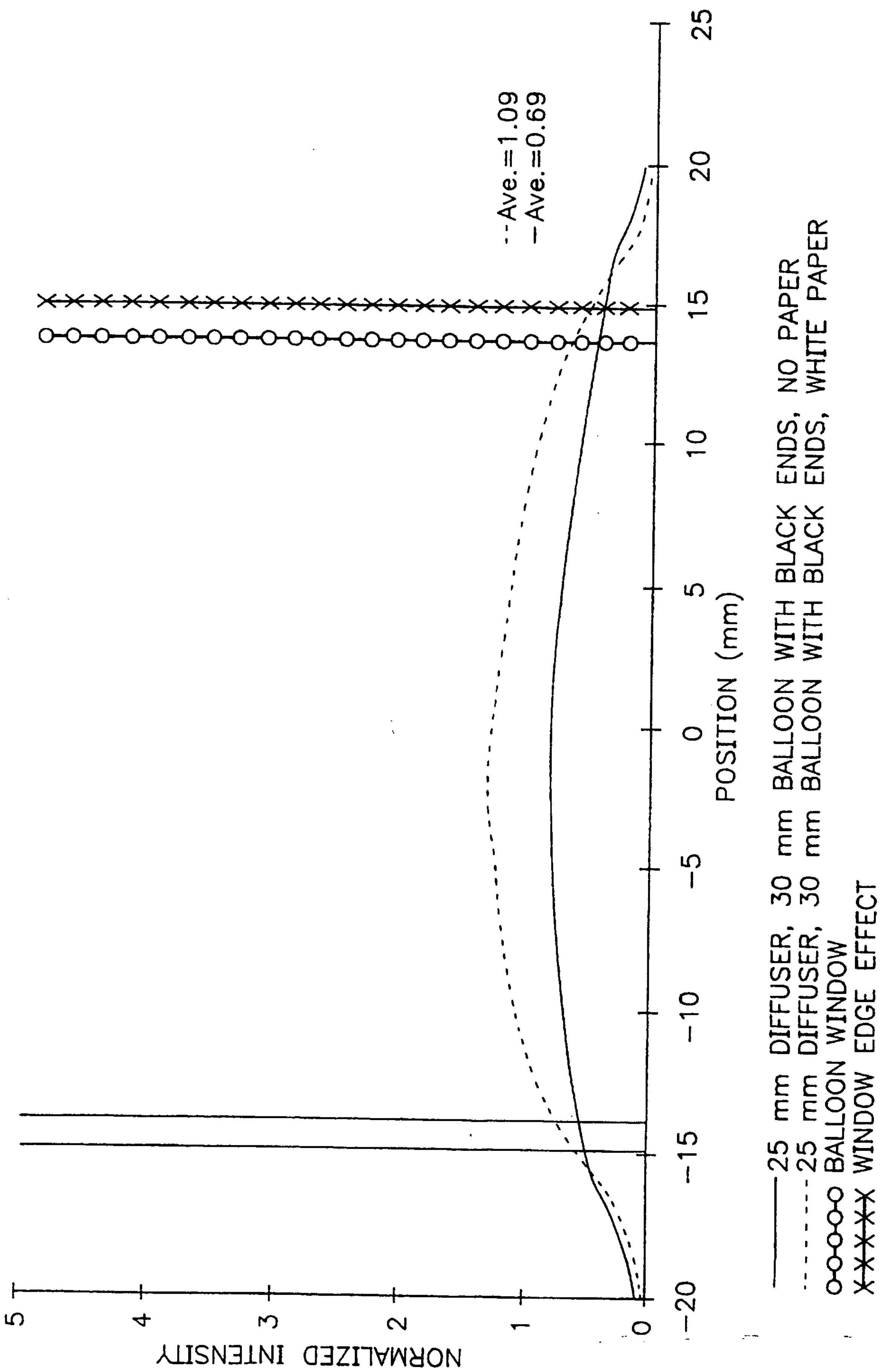

NORMALIZED INTENSITY
0
1
2
3
4
5
−20
−15
−10
−5
0
5
10
15
20
25
POSITION (mm)
--Ave.=1.09
—Ave.=0.69
25 mm DIFFUSER, 30 mm BALLOON WITH BLACK ENDS, NO PAPER
25 mm DIFFUSER, 30 mm BALLOON WITH BLACK ENDS, WHITE PAPER
BALLOON WINDOW
WINDOW EDGE EFFECT

FIG. 2

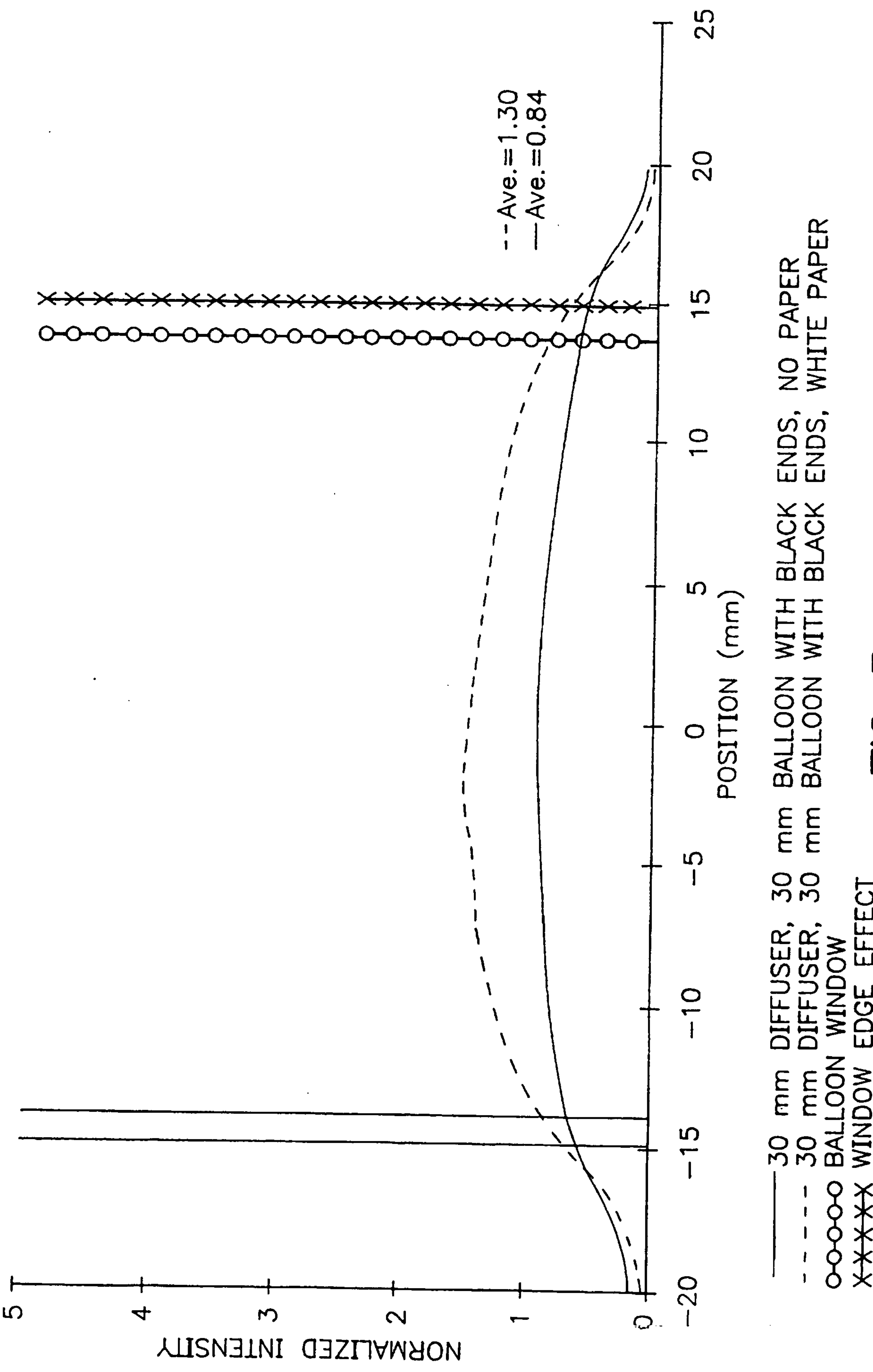

NORMALIZED INTENSITY
0
1
2
3
4
5
POSITION (mm)
-20
-15
-10
-5
0
5
10
15
20
25
- - Ave.=1.30
— Ave.=0.84
—— 30 mm DIFFUSER, 30 mm BALLOON WITH BLACK ENDS, NO PAPER
- - - 30 mm DIFFUSER, 30 mm BALLOON WITH BLACK ENDS, WHITE PAPER
O-O-O-O BALLOON WINDOW
X-X-X-X WINDOW EDGE EFFECT

FIG. 3

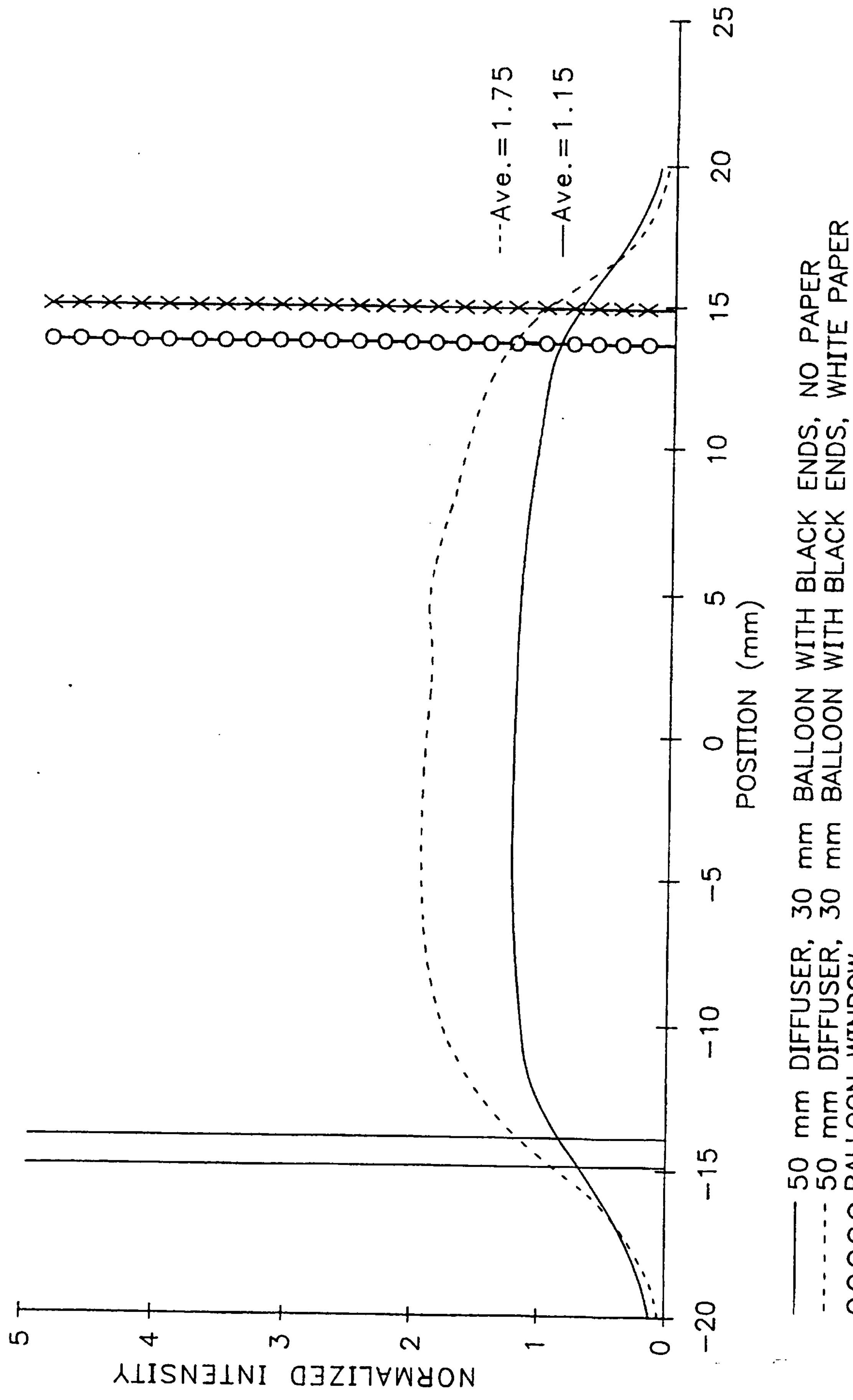

NORMALIZED INTENSITY
0
1
2
3
4
5
POSITION (mm)
−20
−15
−10
−5
0
5
10
15
20
25
---Ave.=1.75
—Ave.=1.15
—— 50 mm DIFFUSER, 30 mm BALLOON WITH BLACK ENDS, NO PAPER
- - - 50 mm DIFFUSER, 30 mm BALLOON WITH BLACK ENDS, WHITE PAPER
o-o-o-o-o BALLOON WINDOW
x-x-x-x-x WINDOW EDGE EFFECT

FIG. 4

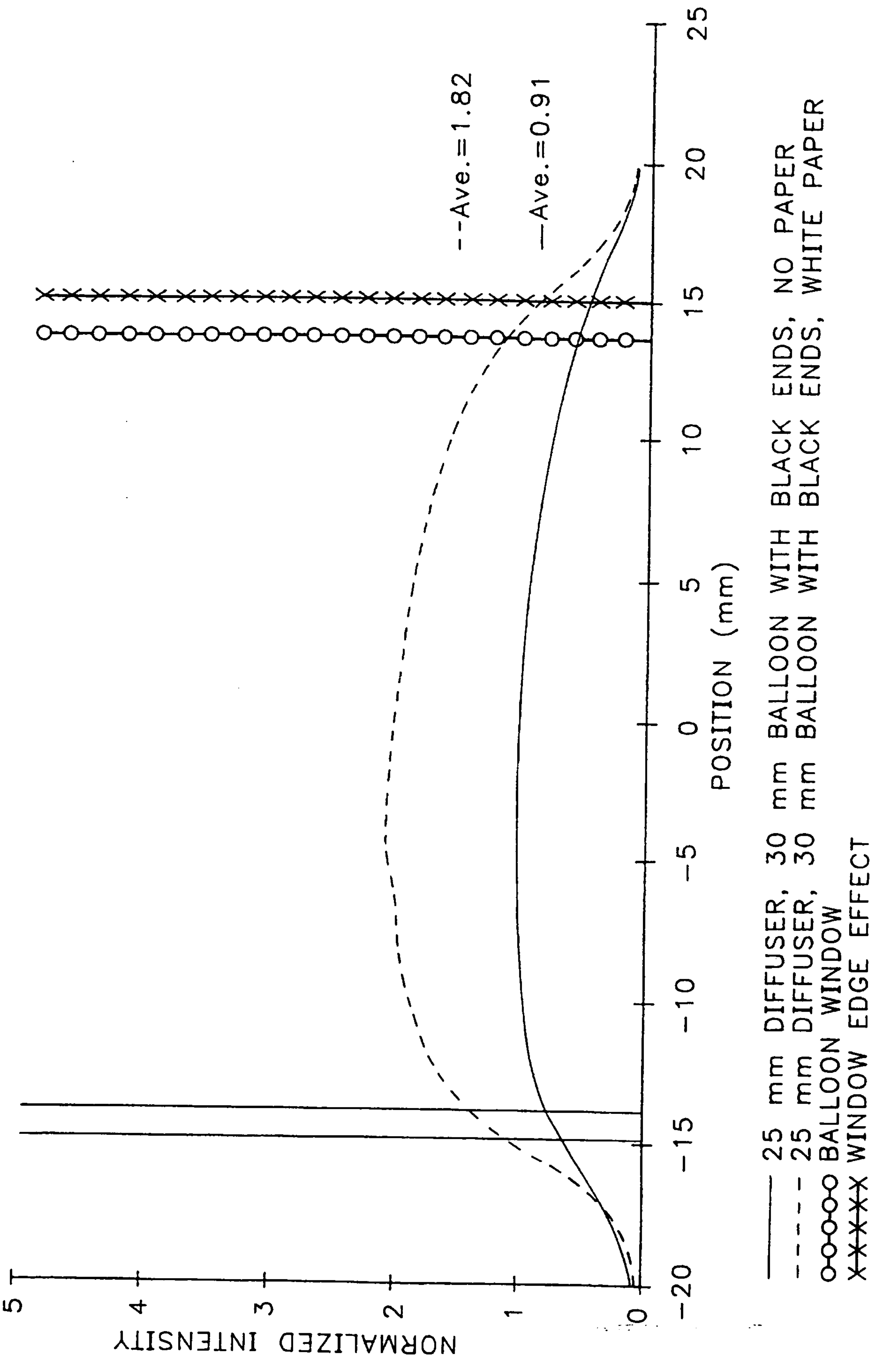

NORMALIZED INTENSITY
0
1
2
3
4
5
POSITION (mm)
−20
−15
−10
−5
0
5
10
15
20
25
- -Ave.=1.82
—Ave.=0.91
—— 25 mm DIFFUSER, 30 mm BALLOON WITH BLACK ENDS, NO PAPER
- - - - 25 mm DIFFUSER, 30 mm BALLOON WITH BLACK ENDS, WHITE PAPER
O-O-O-O-O BALLOON WINDOW
X-X-X-X-X WINDOW EDGE EFFECT

FIG. 5

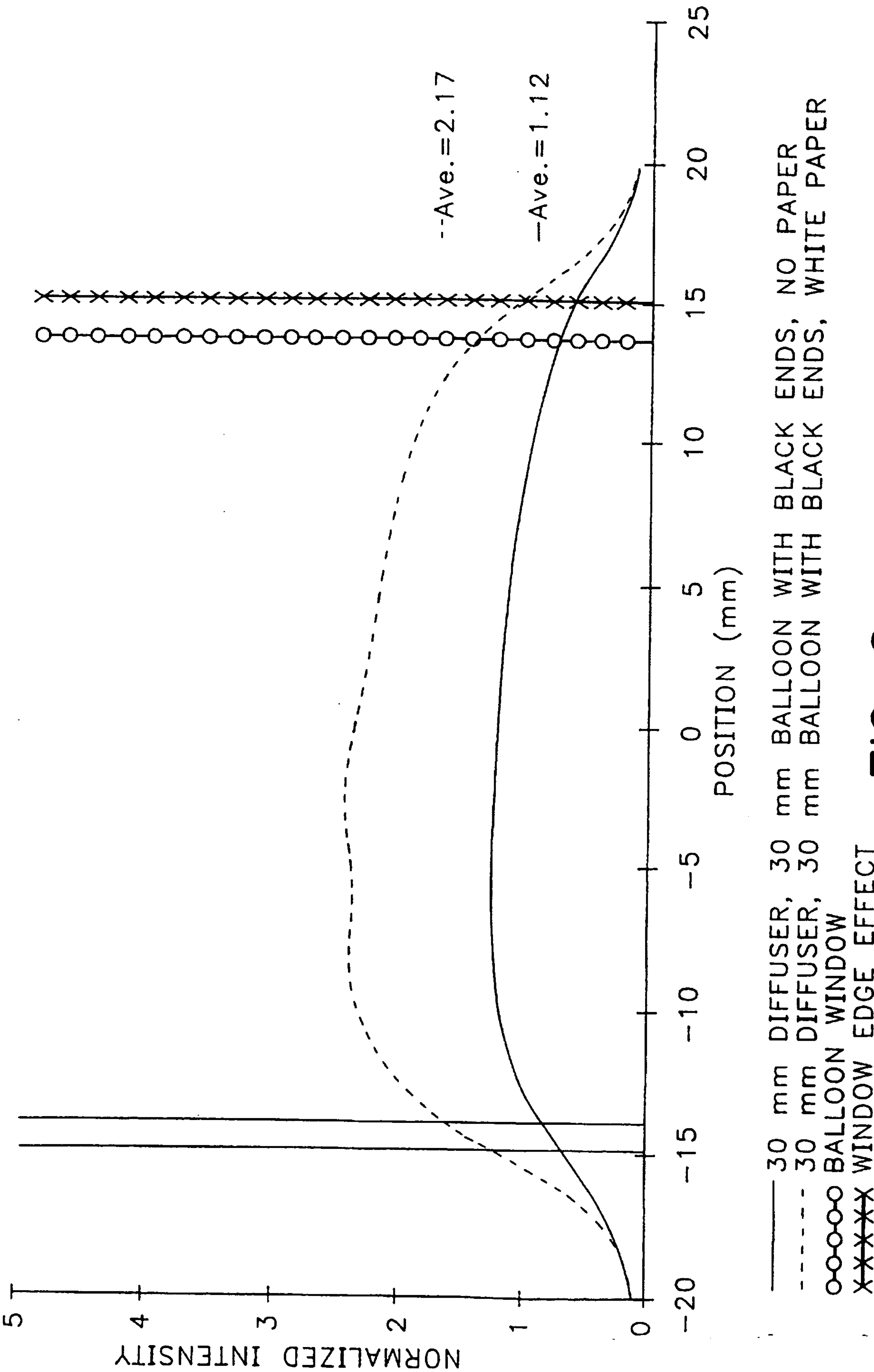
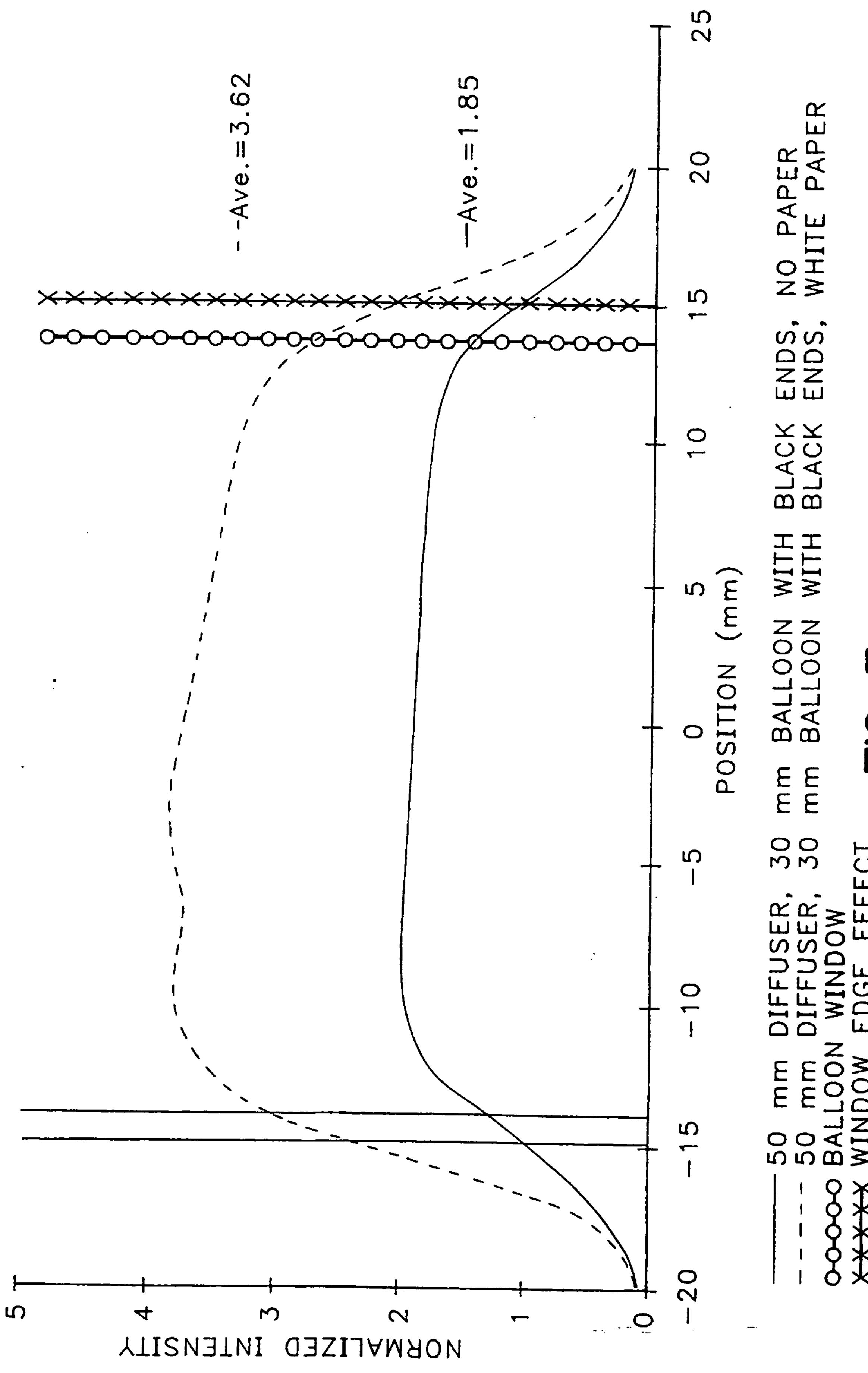
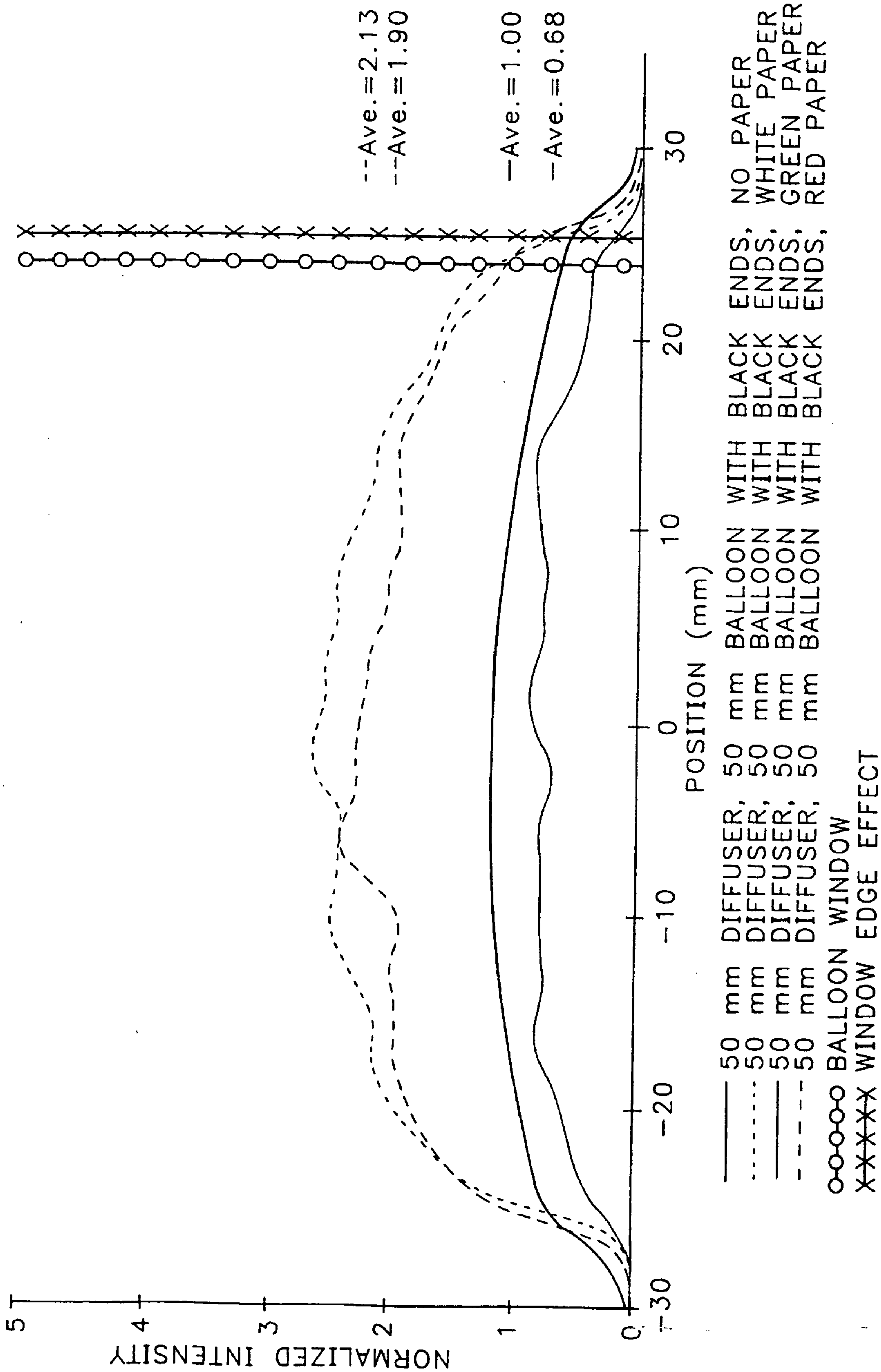

NORMALIZED INTENSITY
0
1
2
3
4
5
POSITION (mm)
−20
−15
−10
−5
0
5
10
15
20
25
- - Ave.=2.17
— Ave.=1.12
—— 30 mm DIFFUSER, 30 mm BALLOON WITH BLACK ENDS, NO PAPER
- - - 30 mm DIFFUSER, 30 mm BALLOON WITH BLACK ENDS, WHITE PAPER
BALLOON WINDOW
WINDOW EDGE EFFECT

FIG. 6



NORMALIZED INTENSITY
0
1
2
3
4
5
POSITION (mm)
−20
−15
−10
−5
0
5
10
15
20
25
- -Ave.=3.62
—Ave.=1.85
——50 mm DIFFUSER, 30 mm BALLOON WITH BLACK ENDS, NO PAPER
- - - 50 mm DIFFUSER, 30 mm BALLOON WITH BLACK ENDS, WHITE PAPER
BALLOON WINDOW
WINDOW EDGE EFFECT

FIG. 7



NORMALIZED INTENSITY
0
1
2
3
4
5
−30
−20
−10
0
10
20
30
POSITION (mm)
Ave.=2.13
Ave.=1.90
Ave.=1.00
Ave.=0.68
50 mm DIFFUSER, 50 mm BALLOON WITH BLACK ENDS, NO PAPER
50 mm DIFFUSER, 50 mm BALLOON WITH BLACK ENDS, WHITE PAPER
50 mm DIFFUSER, 50 mm BALLOON WITH BLACK ENDS, GREEN PAPER
50 mm DIFFUSER, 50 mm BALLOON WITH BLACK ENDS, RED PAPER
BALLOON WINDOW
WINDOW EDGE EFFECT

FIG. 8

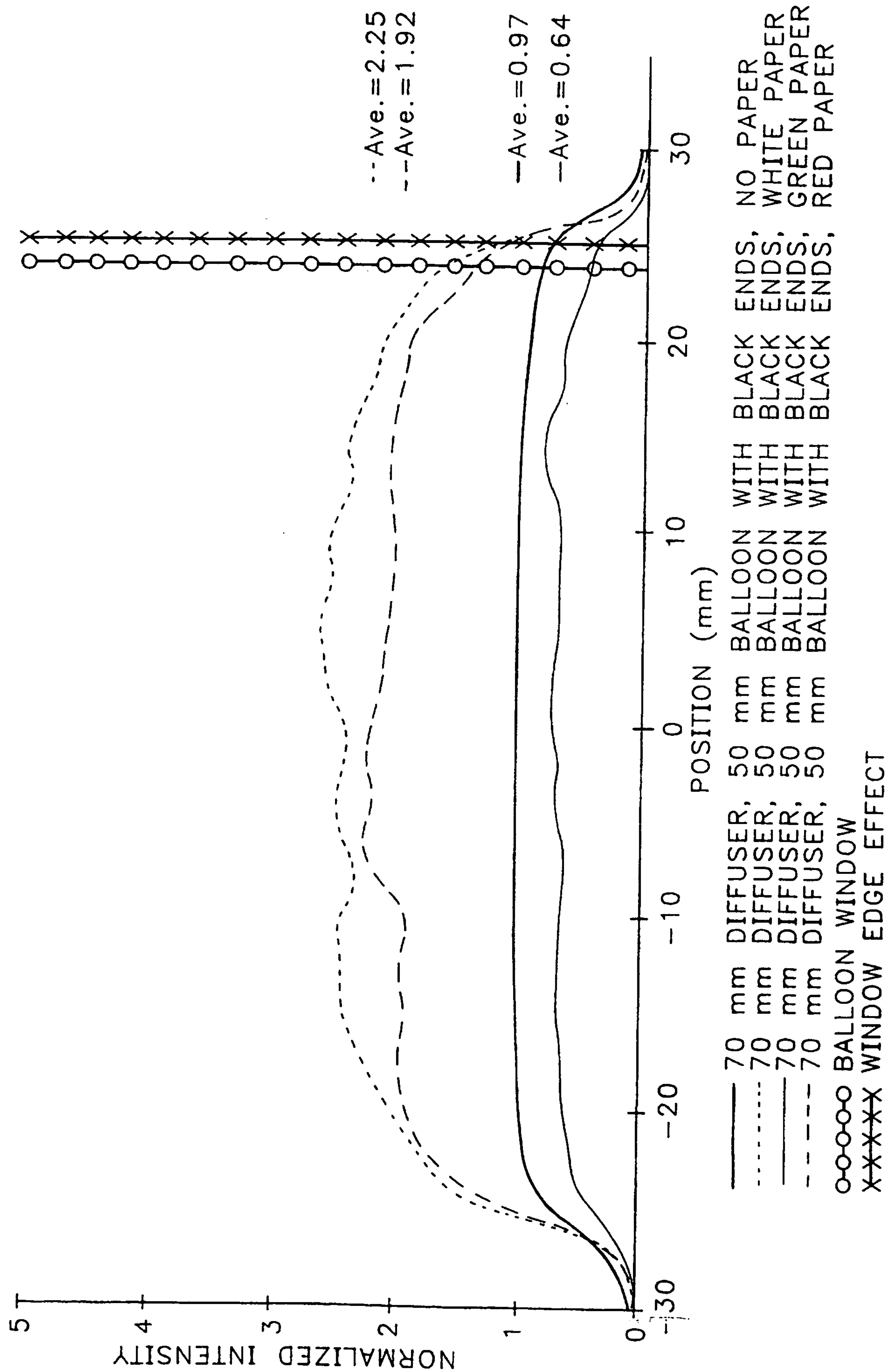

Ave.=2.25
Ave.=1.92
Ave.=0.97
Ave.=0.64
NORMALIZED INTENSITY
0
1
2
3
4
5
−30
−20
−10
0
10
20
30
POSITION (mm)
70 mm DIFFUSER, 50 mm BALLOON WITH BLACK ENDS, NO PAPER
70 mm DIFFUSER, 50 mm BALLOON WITH BLACK ENDS, WHITE PAPER
70 mm DIFFUSER, 50 mm BALLOON WITH BLACK ENDS, GREEN PAPER
70 mm DIFFUSER, 50 mm BALLOON WITH BLACK ENDS, RED PAPER
BALLOON WINDOW
WINDOW EDGE EFFECT

FIG. 9

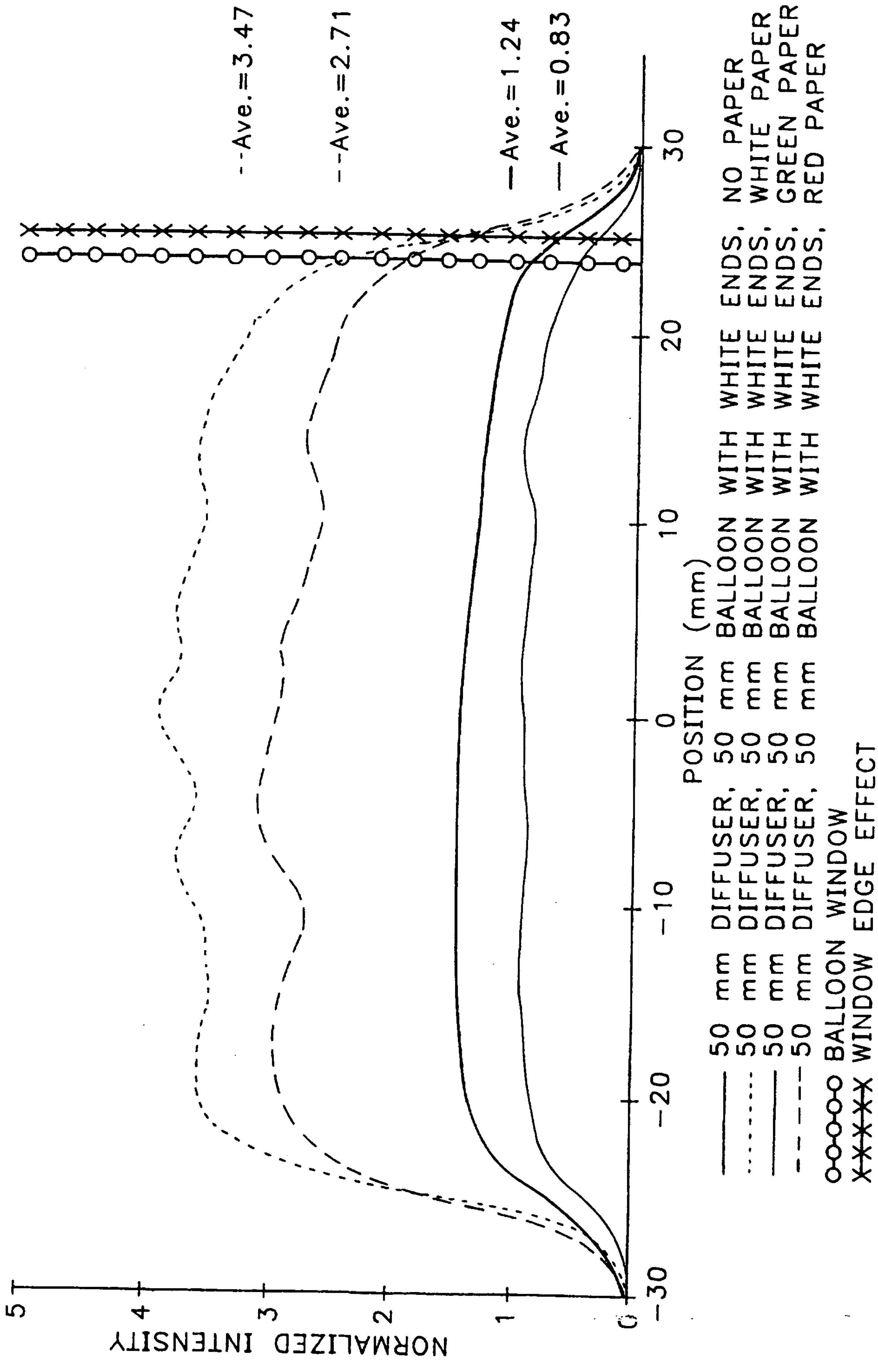
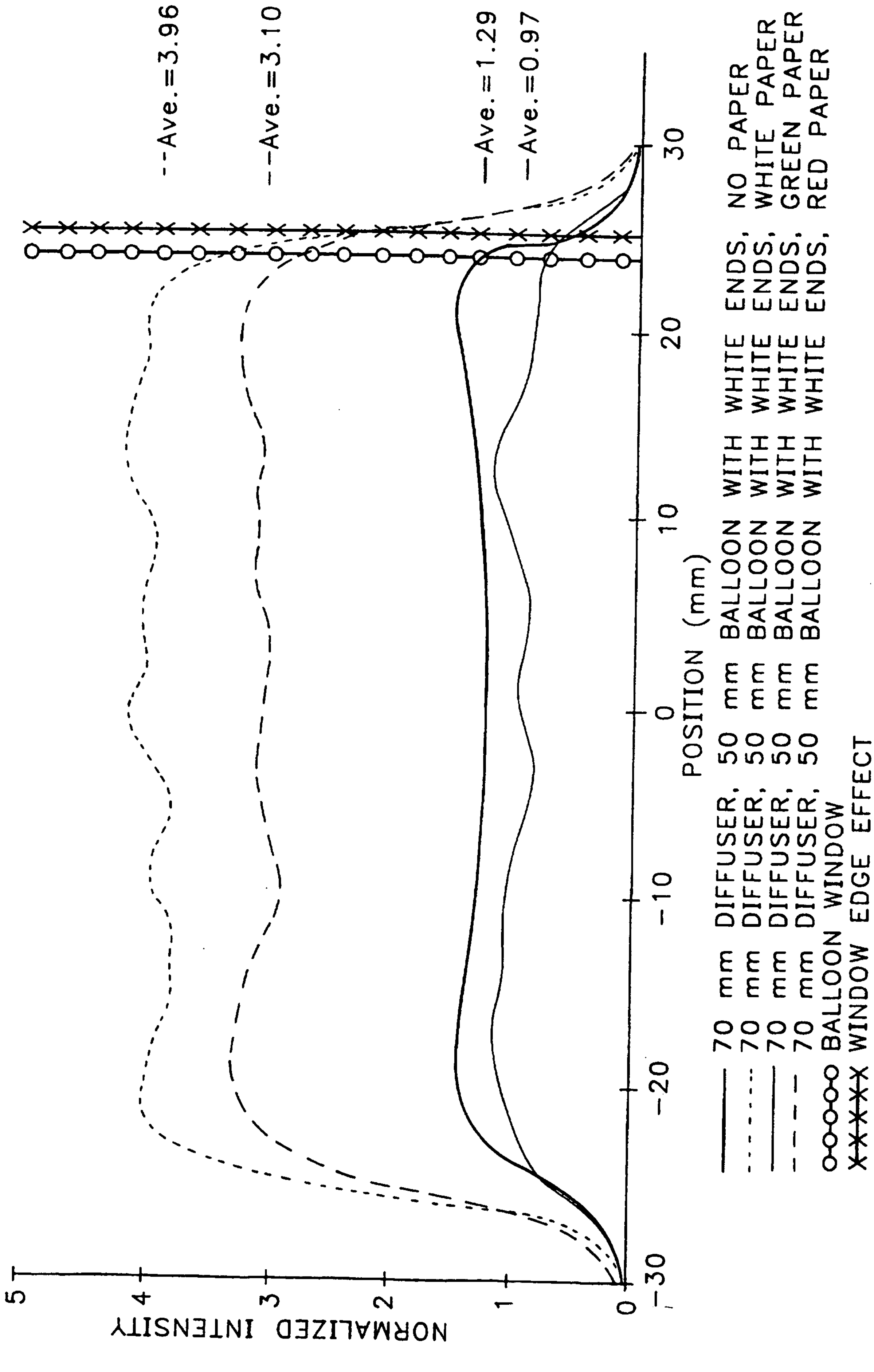

NORMALIZED INTENSITY
0
1
2
3
4
5
POSITION (mm)
-30
-20
-10
0
10
20
30
--Ave.=3.47
--Ave.=2.71
—Ave.=1.24
—Ave.=0.83
50 mm DIFFUSER, 50 mm BALLOON WITH WHITE ENDS, NO PAPER
50 mm DIFFUSER, 50 mm BALLOON WITH WHITE ENDS, WHITE PAPER
50 mm DIFFUSER, 50 mm BALLOON WITH WHITE ENDS, GREEN PAPER
50 mm DIFFUSER, 50 mm BALLOON WITH WHITE ENDS, RED PAPER
BALLOON WINDOW
WINDOW EDGE EFFECT

FIG. 10



NORMALIZED INTENSITY
0
1
2
3
4
5
POSITION (mm)
−30
−20
−10
0
10
20
30
--Ave.=3.96
--Ave.=3.10
—Ave.=1.29
—Ave.=0.97
70 mm DIFFUSER, 50 mm BALLOON WITH WHITE ENDS, NO PAPER
70 mm DIFFUSER, 50 mm BALLOON WITH WHITE ENDS, WHITE PAPER
70 mm DIFFUSER, 50 mm BALLOON WITH WHITE ENDS, GREEN PAPER
70 mm DIFFUSER, 50 mm BALLOON WITH WHITE ENDS, RED PAPER
BALLOON WINDOW
WINDOW EDGE EFFECT

FIG. 11

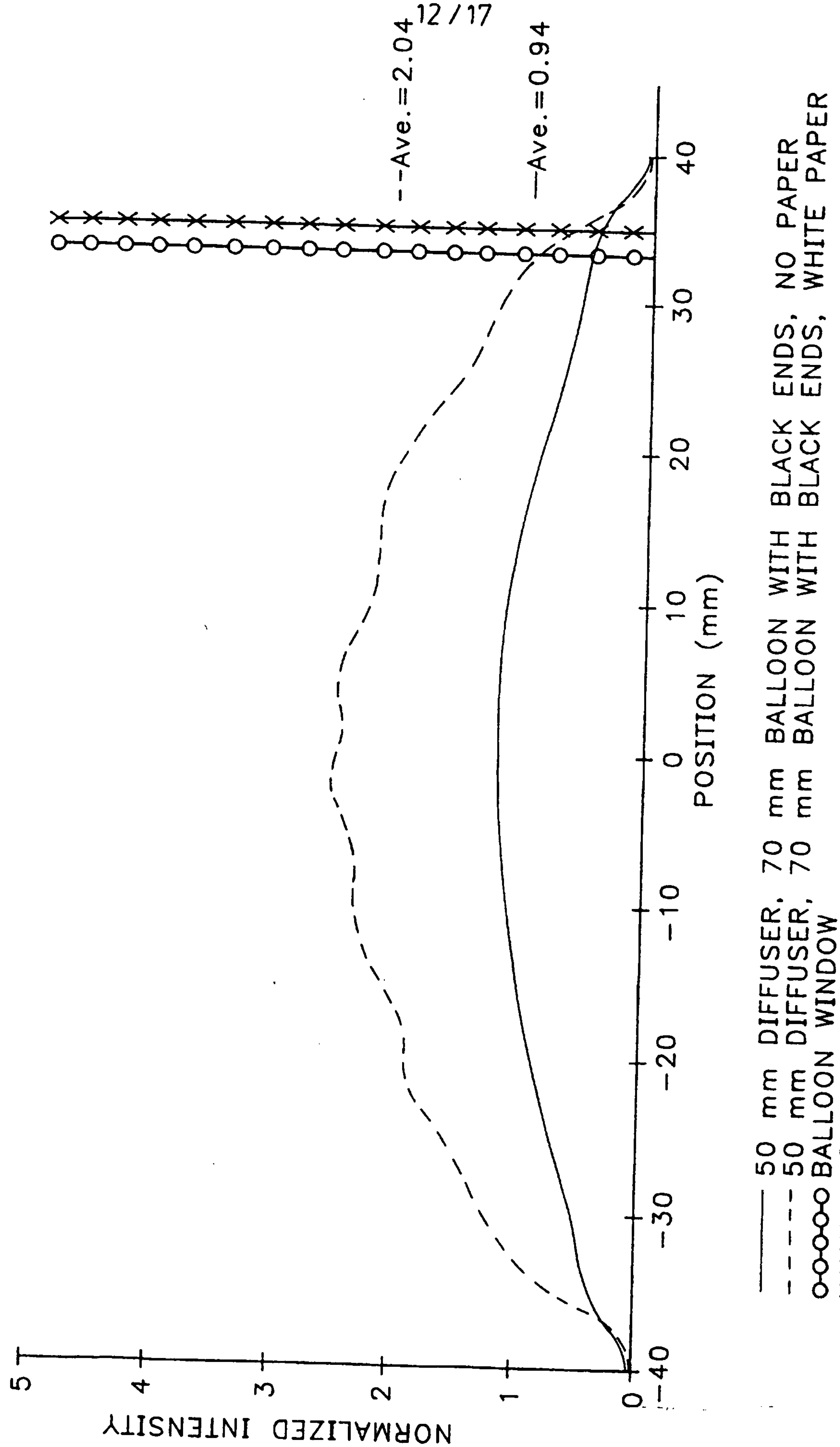

--Ave.=2.04
—Ave.=0.94
NORMALIZED INTENSITY
0
1
2
3
4
5
-40
-30
-20
-10
0
10
20
30
40
POSITION (mm)
—— 50 mm DIFFUSER, 70 mm BALLOON WITH BLACK ENDS, NO PAPER
- - - 50 mm DIFFUSER, 70 mm BALLOON WITH BLACK ENDS, WHITE PAPER
o-o-o-o BALLOON WINDOW
x-x-x-x WINDOW EDGE EFFECT

FIG. 12

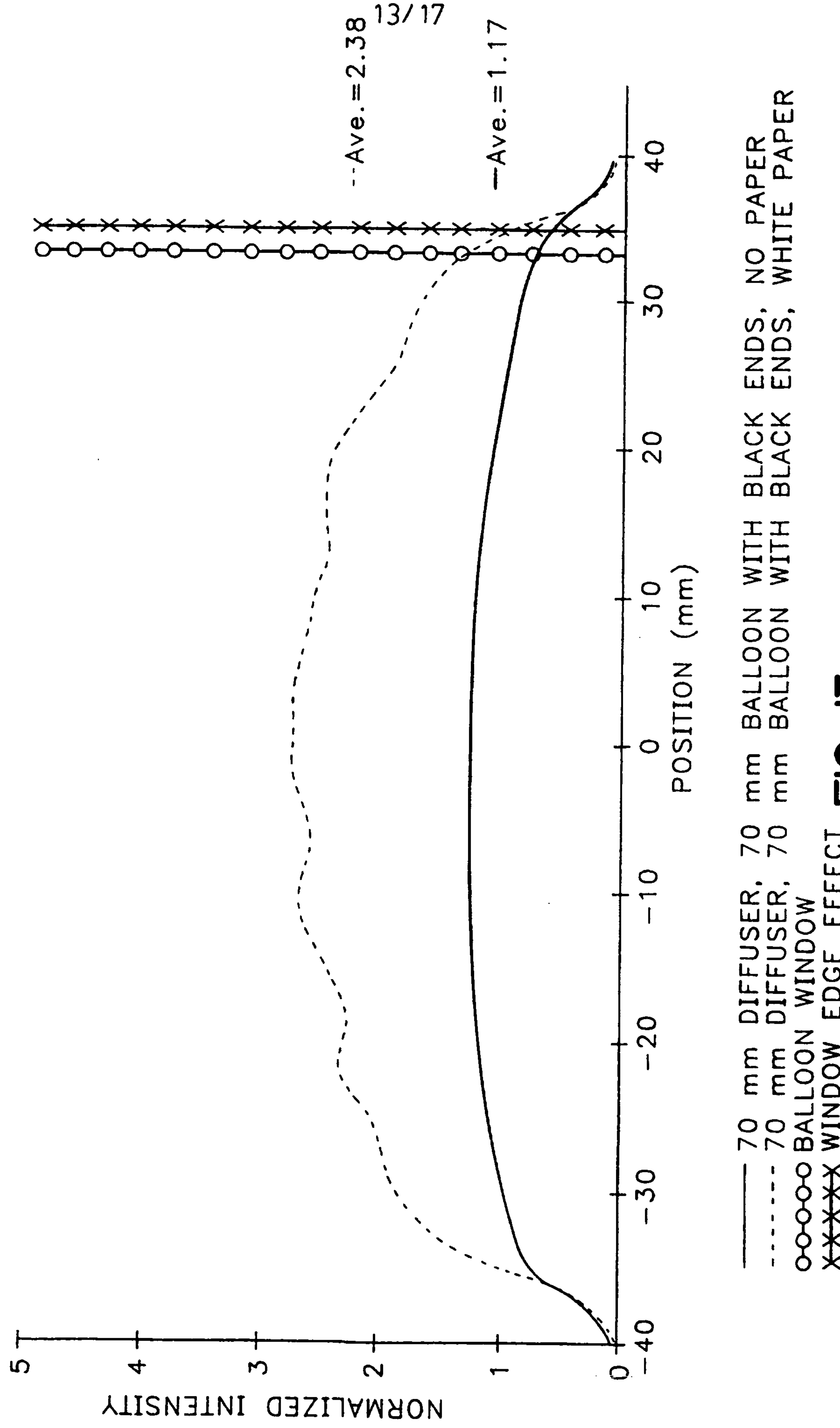

NORMALIZED INTENSITY
0
1
2
3
4
5
-40
-30
-20
-10
0
10
20
30
40
POSITION (mm)
Ave.=2.38
Ave.=1.17
70 mm DIFFUSER, 70 mm BALLOON WITH BLACK ENDS, NO PAPER
70 mm DIFFUSER, 70 mm BALLOON WITH BLACK ENDS, WHITE PAPER
BALLOON WINDOW
WINDOW EDGE EFFECT

FIG. 13

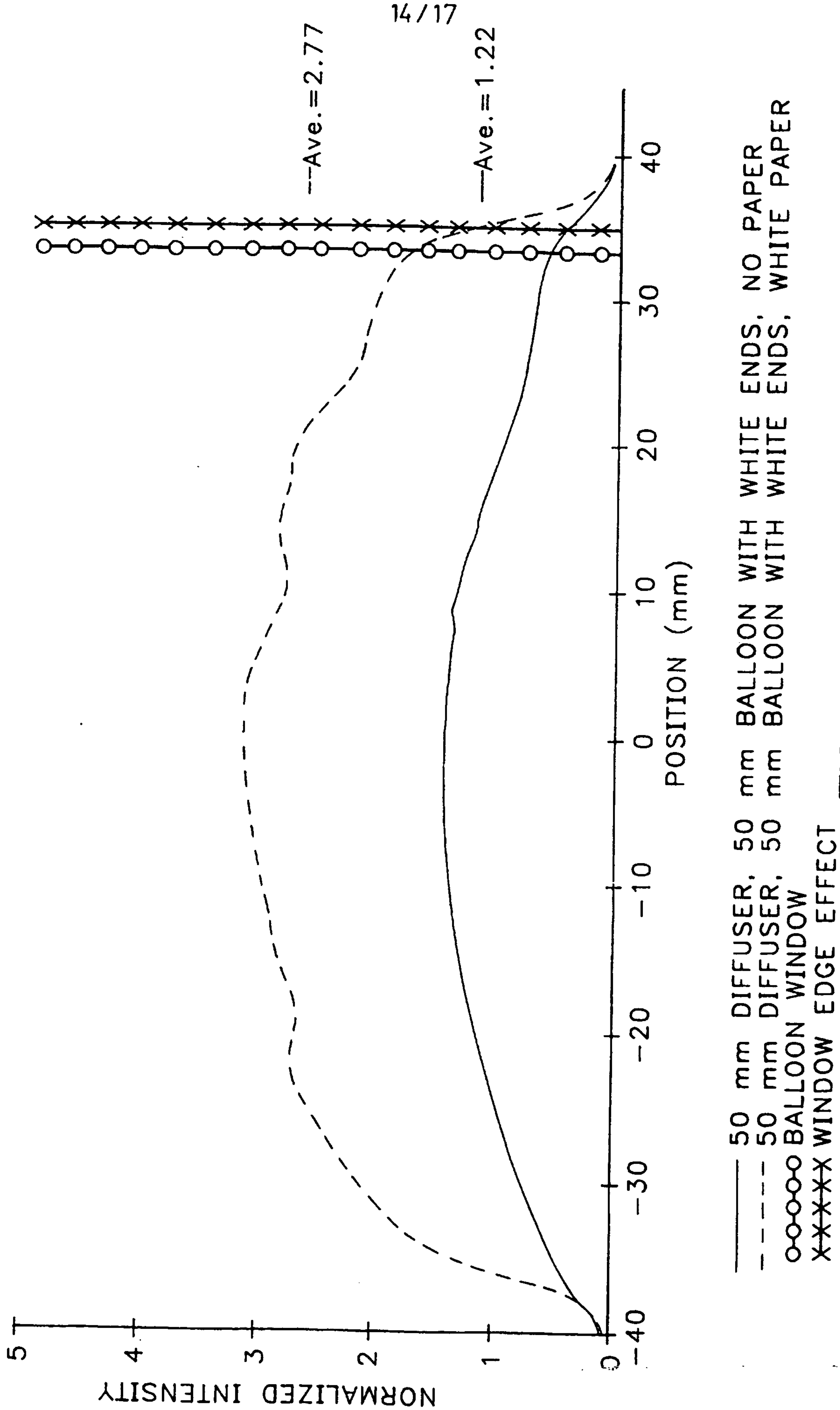

—Ave.=2.77
—Ave.=1.22
NORMALIZED INTENSITY
0
1
2
3
4
5
−40
−30
−20
−10
0
10
20
30
40
POSITION (mm)
——— 50 mm DIFFUSER, 50 mm BALLOON WITH WHITE ENDS, NO PAPER
– – – 50 mm DIFFUSER, 50 mm BALLOON WITH WHITE ENDS, WHITE PAPER
O-O-O-O BALLOON WINDOW
X-X-X-X WINDOW EDGE EFFECT

FIG. 14

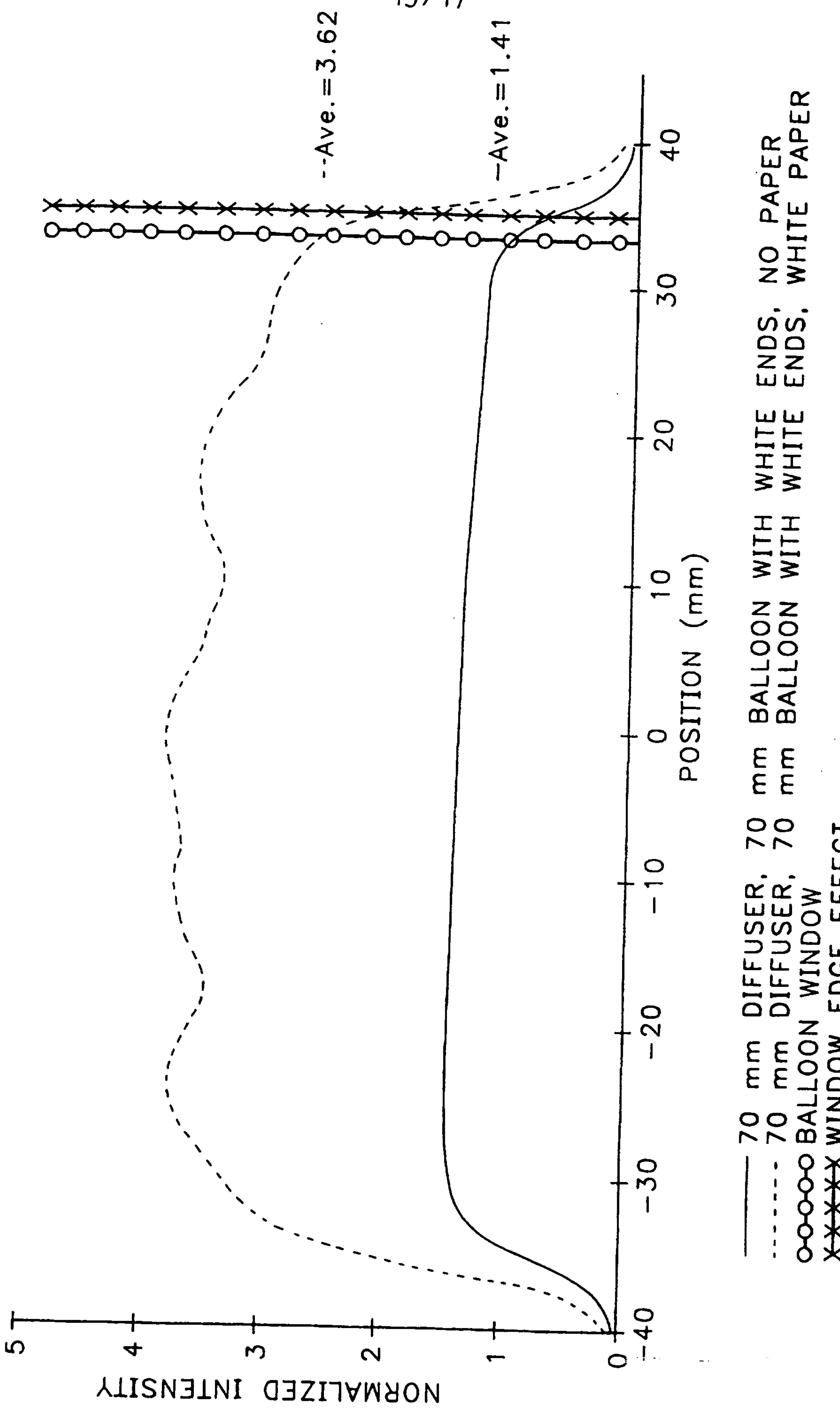

Ave.=3.62
Ave.=1.41
NORMALIZED INTENSITY
0
1
2
3
4
5
POSITION (mm)
-40
-30
-20
-10
0
10
20
30
40
70 mm DIFFUSER, 70 mm BALLOON WITH WHITE ENDS, NO PAPER
70 mm DIFFUSER, 70 mm BALLOON WITH WHITE ENDS, WHITE PAPER
BALLOON WINDOW
WINDOW EDGE EFFECT

FIG. 15

FIG. 16

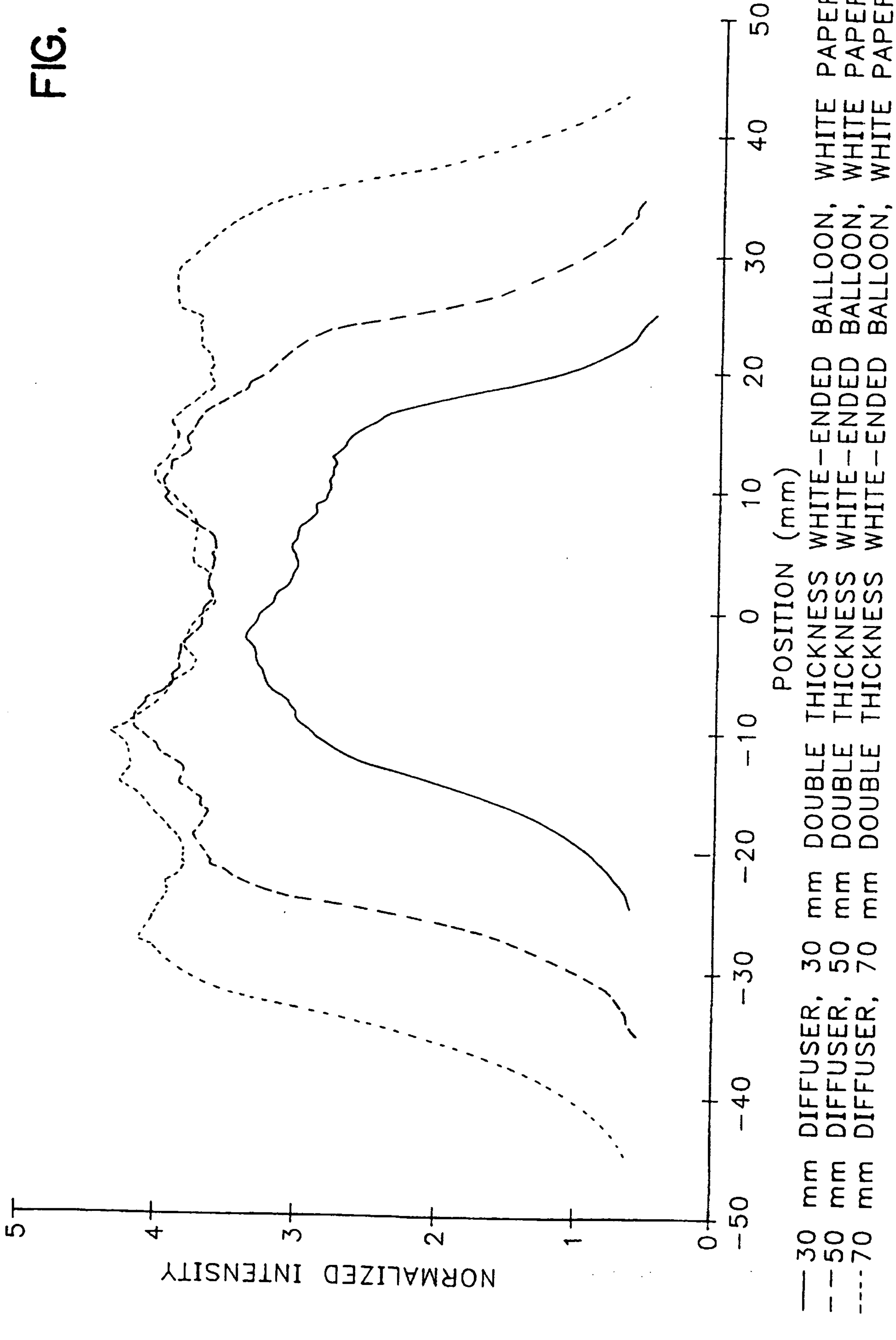
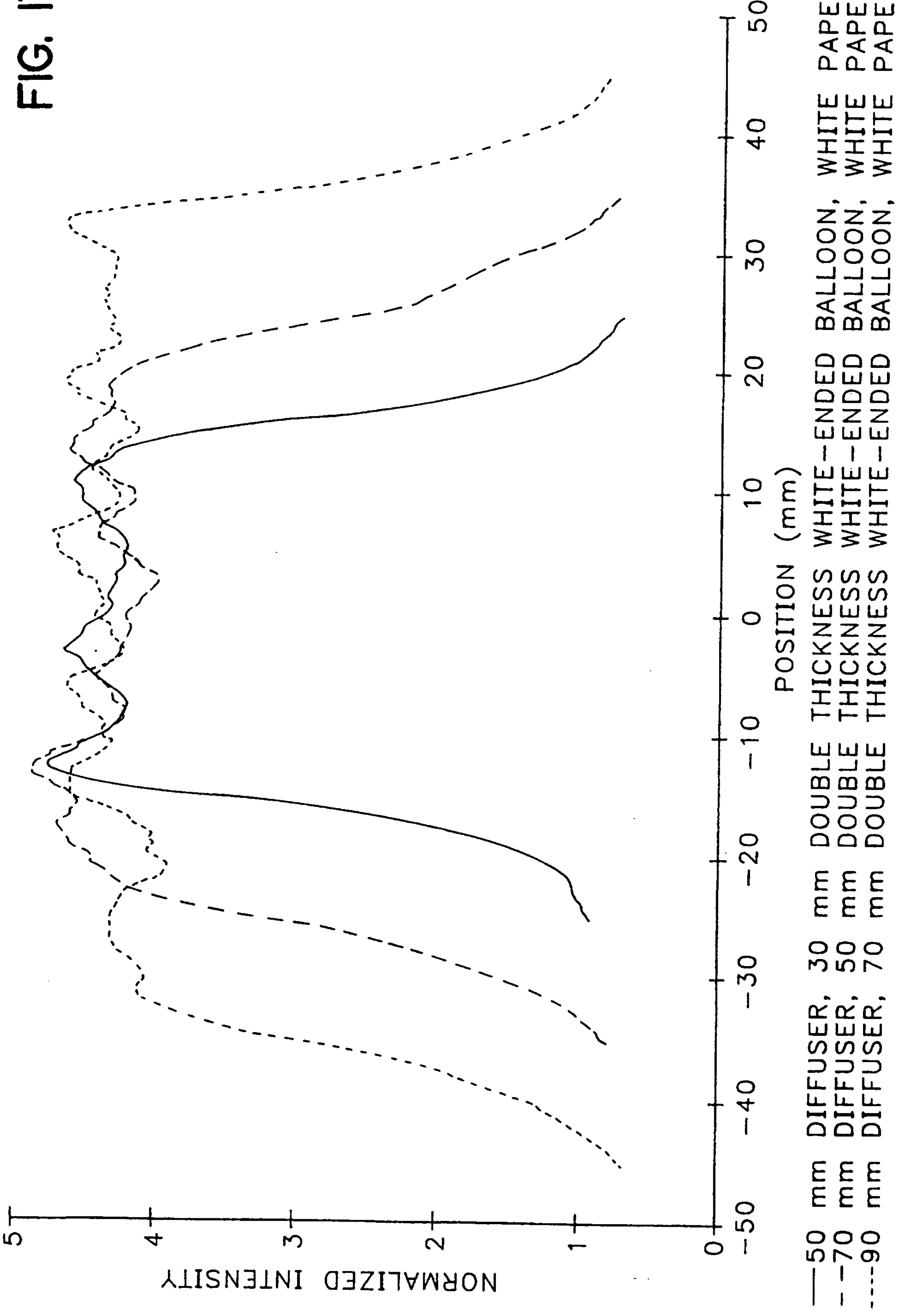

NORMALIZED INTENSITY
0
1
2
3
4
5
POSITION (mm)
−50
−40
−30
−20
−10
0
10
20
30
40
50
— 30 mm DIFFUSER, 30 mm DOUBLE THICKNESS WHITE−ENDED BALLOON, WHITE PAPER
– – 50 mm DIFFUSER, 50 mm DOUBLE THICKNESS WHITE−ENDED BALLOON, WHITE PAPER
---- 70 mm DIFFUSER, 70 mm DOUBLE THICKNESS WHITE−ENDED BALLOON, WHITE PAPER

FIG. 17


NORMALIZED INTENSITY
0
1
2
3
4
5
POSITION (mm)
-50
-40
-30
-20
-10
0
10
20
30
40
50
—50 mm DIFFUSER, 30 mm DOUBLE THICKNESS WHITE-ENDED BALLOON, WHITE PAPER
- -70 mm DIFFUSER, 50 mm DOUBLE THICKNESS WHITE-ENDED BALLOON, WHITE PAPER
----90 mm DIFFUSER, 70 mm DOUBLE THICKNESS WHITE-ENDED BALLOON, WHITE PAPER

INTERNATIONAL SEARCH REPORT

Intern al Application No
PCT/CA 97/00337

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61B17/36 A61N5/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61B A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 0 411 132 A (S.L.T.JAPAN CO,LTD) 6 February 1991 see column 6, line 11 - line 21	1-15
Y	WO 90 00914 A (ROWLAND) 8 February 1990 cited in the application see claims 1-5	1-15
A	EP 0 448 004 A (WEIKL ET AL.) 25 September 1991 see column 8, line 37 - line 57	1,5
A	EP 0 311 458 A (BARD) 12 April 1989 see column 14, line 4 - line 6	1

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

2

Date of the actual completion of the international search	Date of mailing of the international search report
28 July 1997	01.08.97

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax (+ 31-70) 340-3016	Glas, J

INTERNATIONAL SEARCH REPORT

In ational application No.
PCT/CA 97/00337

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 16-19
because they relate to subject matter not required to be searched by this Authority, namely:
PCT Rule 39.1 (iv) Method for treatment of the human body by surgery or therapy

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Internal Application No
PCT/CA 97/00337

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 411132 A	06-02-91	JP 2098373 A	10-04-90
		AT 122246 T	15-05-95
		AU 4338889 A	01-05-90
		CA 2000189 A	05-04-90
		DE 68922607 D	14-06-95
		DE 68922607 T	30-11-95
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WO 9000914 A	08-02-90	AU 4032389 A	19-02-90
EP 448004 A	25-09-91	DE 9003184 U	18-07-91
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